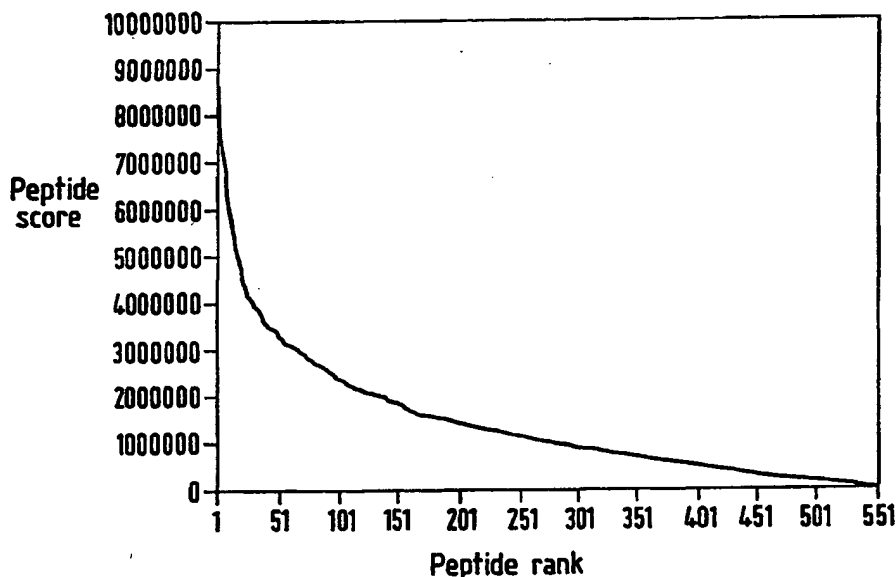




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(54) Title: IDENTIFICATION OF MHC BINDING PEPTIDES**(57) Abstract**

The invention provides a method for the prediction of the binding affinity of a peptide to a major histocompatibility (MHC) class II molecules comprising: 1) ascertaining the characteristics of a MHC molecule binding groove, 2) presenting a selected peptide to the MHC molecule and ascertaining a first conformation score for each pocket bound peptide side-chain, 3) amending the conformation of each pocket bound peptide side-chain and ascertaining a second conformation score, 4) repeating step 3 with alternative conformations of each peptide pocket bound side-chain, 5) choosing the highest conformation score for each pocket bound peptide side-chain in each binding groove pockets, herein known as "the pocket", and 6) combining the highest conformation score for each pocket and ascertaining a binding score for the complete peptide.

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it is believed that the backbone structure of all MHC class II alleles presently identified are similar to that of HLA-DR1. Structures of different alleles can be predicted by using homology modelling. This involves identifying the amino acid differences near the binding groove and using a computer to change the conformation of the side-chains to give favourable steric and electrostatic arrangements and to make the pockets as large as possible. The end result is a three dimensional structure of a MHC class II molecule, which can be used in various experiments.

The ability to predict the peptides in a protein which can bind to a given MHC molecule has great value especially for medical applications. It is known, for example, that in certain auto-immune diseases, T cells react with self-peptides presented by MHC class II molecules. It would be valuable to predict which peptides from auto-immune proteins are presented by MHC class II molecules in these diseases as well as to predict the binding of analogues of these peptides synthesised as potential antagonists for the presentation of self-peptides. In the selection of peptides for synthetic vaccines, the ability to predict MHC class II binding peptides would be advantageous. In addition, where heterologous proteins are developed as medicines or diagnostic imaging agents, it would be advantageous to predict potential MHC class II binding peptides in order to eliminate these from the heterologous proteins before administration to patients.

While studies of peptides complexed with MHC class I molecules have revealed conserved "anchor" residues at certain positions within the presented peptides, such studies with peptides complexed with MHC class II molecules have been less successful mainly because of the greater length variability of such peptides and the consequent difficulty in aligning their sequences.

Methods for accurately predicting the binding potential of

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peptides have been restricted to MHC class I interaction with a peptide. In one method using three-dimensional structures of MHC class I molecules, peptide binding is ranked in ascending order according to the energy values determined.

5 This method requires that the MHC structure be known, or that there is an obvious molecular model for the MHC structure. An identical method is said to be available for MHC class II but it does not consider the longer average length of the peptide and the open-ended peptide binding groove of MHC class
10 II molecules. Neither does it use the best potential conformation of peptide amino acid side-chains and, therefore the binding energies calculated are only approximations.

Another drawback of using the same method for MHC class I and
15 MHC class II peptide binding is that the binding of peptides to MHC class II is less dependant on strict allele-specific binding motifs than peptides binding to MHC class I. Individual amino acids in the peptide play a more significant role in MHC class II binding than MHC class I such that the
20 conformation of amino acid side-chains is proportionally more important to the accuracy of binding analysis. Therefore, known methods do not provide a general method for analysing the binding of peptides to three-dimensional structures of MHC class II. There is thus a need for improved methods for
25 predicting the MHC class II binding potential of peptides.

An object of this invention is to provide a method for accurately predicting the binding affinity of a peptide fragment binding to a MHC class II molecule.

30

Another object of this invention is to provide a computer conditioned to perform the task of predicting the binding affinity of a peptide fragment binding to a MHC class II molecule.

35

A yet further object of this invention is to provide a vaccine derived from the peptide fragment whose binding affinity to

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MHC class II molecules has been determined.

Another object of this invention is to provide a pharmaceutical composition which comprises a peptide whose
5 binding affinity to MHC class II molecules has been determined.

According to the first aspect of this invention, there is provided a method for the prediction of the binding affinity
10 of a peptide and a major histocompatibility (MHC) class II molecules comprising;

- 1) ascertaining the characteristics of a MHC molecule binding groove,
- 2) presenting a selected peptide to the MHC molecule and
15 ascertaining a first conformation score for each pocket bound peptide side-chain,
- 3) amending the conformation of each pocket bound peptide side-chain and ascertaining a second conformation score,
- 4) repeating step 3 with alternative conformations of each
20 peptide pocket bound side-chain,
- 5) choosing the highest conformation score for each pocket bound peptide side-chain,
- 6) combining the highest conformation score for each pocket-bound peptide side-chain and then ascertaining a binding score
25 for the peptide.

It is particularly desirable to then compile information on all peptide fragments in a protein and compare the binding scores. It is preferable if the conformation of the backbone
30 of the peptide fragment is also altered and the conformation score and the binding score is then reassessed.

The method of this invention thus involves assessing a binding score for all possible candidate peptides by considering the
35 predicted three-dimensional conformations and interactions between the MHC and the peptide in the complex. The computed score indicates the predicted binding affinity for the

- 5 -

particular peptide binding with the MHC allele and can be used to predict whether the peptides are likely to bind, or not.

Preferably, the conformation score for each pocket bound peptide side-chain is ascertained by considering at least one of the following parameters:

- a) the steric overlap between the pocket bound peptide residue bound in the pocket and an atom forming the pocket; this is value B,
- 10 b) the number of hydrogen bonds which can be formed between the pocket bound peptide residue and an atom forming the pocket; this is value C,
- c) the strength of electrostatic interactions between any polar atoms of the pocket bound peptide residue and any polar
- 15 atoms forming the pocket; this is value D, and
- d) the number of favourable contacts between the pocket bound peptide residue and the MHC residues forming one of the pockets; this is value E.

20 The conformation score for each peptide is computed based upon the predicted atomic interactions between each of the pocket bound peptide residues and MHC pockets. The geometric constraints imposed on the peptide by the shape of the MHC binding groove play an important part of the scoring function.

25 Favourable packing arrangements between peptide and MHC side-chains are rewarded by the scoring function, whilst arrangements involving steric overlap are penalised. Alternative conformation are tried for MHC residues if an MHC residue overlaps with a peptide side chain.

30

If no preferable conformation can be found the MHC side-chain is returned to its original conformation. In the event of more than a pocket residue side-chain overlapping with a pocket bound peptide side chain, the pocket residue side

35 chains are adjusted in order of overlap severity, with the pocket residue side-chain which has the most severe overlap being adjusted first.

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In preferred embodiments the steric overlap between the pocket bound peptide residue and the atoms forming the pocket can not be greater than 0.35 Angstroms, otherwise the residue is deemed unable to fit in the pocket.

5

Conveniently a favourable contact occurs when an atom from an MHC residue and an atom from the peptide residue have their centres separated by no more than the sum of their radii plus 0.5 Angstroms and are not overlapping.

10

Preferably the values B to E are imported into a first equation to give a conformation score(Z). The first equation is $Z_n = (cK_2C) - (cK_3D) + (cK_4E) - (cK_1B)$, where cK_1 to cK_4 are constants and n is the number of the pocket.

15

The value of cK_1 is between 50 and 150. Preferably between 75 and 125.

The value of cK_2 is between 1000 and 2000. Preferably between

20 1250 and 1750.

The value of cK_3 is between 250 and 750. Preferably between 350 and 650.

25 The value of cK_4 is between 500 and 1500. Preferably between 750 and 1250.

Conveniently the Z_n value for a pocket is multiplied by a coefficient, L, depending on the pockets importance in
30 binding, to give a second Z_n value. The value L is in the range of 0.001 to 5. Larger pockets are considered more important in determining which peptide can bind, compared with the other smaller pockets, so the scores contributed by each pocket are weighted in proportion to the amount of the peptide
35 side-chain buried by the surface of the MHC molecule. When binding to MHC class II molecules, peptides have shown high similarity in the degree to which their side-chains are buried

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by the MHC surface, despite having dissimilar sequences.

Preferably all the Z_n values are summed to give a value J. Value J is the overall contributing score of all the pockets for a certain conformation of the peptide fragment.

Conveniently the MHC residue is paired with the pocket-bound peptide residue if an atom from the MHC residue and an atom from the pocket-bound peptide residue have their centres separated by no more than the sum of their van der Waal radii plus one Angstrom.

In a preferred embodiment a value A_n is calculated by summing the pairwise interaction frequencies of paired residues. As for the Z_n value, preferably the value A_n for a pocket is multiplied by a coefficient, X, depending on the pockets importance in binding. Preferably X is between 0.001 and 5.

Conveniently the A_n value for the pockets are summed to give a value P.

In a preferred embodiment the binding score is ascertained by at least one of the following parameters

- a) the number of groove-bound hydrophobic residues; this is value F,
- b) the number of non groove-bound hydrophilic residues; this is value G,
- c) the number of peptide residues deemed to fit within their respective binding pocket; this is value H.

Preferably values F, G, H, J and P are imported into a second equation to give a first binding score, Y.

Conveniently the second equation is $Y = J * F^2 * (G * H + 1) + P$.

However, in the alternative, the term H_e , which evaluates the hydrophobicity of the pocket bound peptide side chains using

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a hydrophobicity scale disclosed in Janin et al [1979] Nature, 277 pg 491, can also be used to determine the Y value. Accordingly, $Y = (bK_2C) - (bK_3D) + (bK_4E) - (bK_1B) + (bK_5He) + P$. The scale used in Janin et al to measure hydrophobicity has a range from
5 -1.8 for lysine to 0.9 for cysteine.

It is known that peptides having favourable hydrophobic/hydrophobic interactions with solvent and MHC atoms have a higher binding affinity. Accordingly, it is
10 preferable to include the term He.

The value of bK_1 is between 1 and 10. Preferably between 1 and 5.

15 The value of bK_2 is between 20 and 60. Preferably between 30 and 50.

The value of bK_3 is between 300 and 900. Preferably between 450 and 750.

20

The value of bK_4 is between 1 and 20. Preferably between 5 and 15.

The value of bK_5 is in between 1 and 800. Conveniently
25 between 100 and 600. Preferably between 100 and 400.

In a preferred embodiment determination of the conformation score and the binding score are repeated for each pocket and each conformation of the peptide residue in said pocket. The
30 conformation of the peptide is altered by rotating a side chain of the peptide residue by a pre-determined amount. In this way all possible conformations of the peptide side-chain in the pocket can be studied and the best or most likely conformation can be chosen to obtain the binding score.

35

The conformation of the backbone of the peptide fragment is changed by modelling the conformation of the backbone on any

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one of 167 backbones which have been previously generated, based on human and murine crystallographic structures of MHC class II peptide complexes. The backbone conformation and the conformation of the peptide fragment side chains are altered systematically until the conformation score and the binding score of every possible conformation has been determined.

Conveniently the steps are repeated using different peptides from a protein.

10

In preferred embodiments the binding scores (Y) for different peptides are tabulated and compared. Peptides with the highest scores are predicted to have the highest binding affinity for the particular MHC allele.

15

In a preferred embodiment the method of determining the binding affinity of a peptide residue for an MHC class II molecule is used in the manufacture of a vaccine derived from a peptide identified by said method.

20

Preferably the method of determining the binding affinity of a peptide residue for an MHC class II molecule is used to remove potentially immunogenic sequences from a protein and thus reduce said proteins immunogenicity when administered to an organism.

25

Using the afore-detailed method it is possible to predict the peptides from an auto-immune protein which are presented by MHC class II molecules. Thereafter, it is possible to synthesise peptides which would be antagonists to the presentation of such peptides by the MHC class II molecules. It is also possible to determine any proteins in a vaccine containing heterologous proteins which might result in the stimulation of T cells due to their presentation on MHC class II molecules. These proteins could then be altered or removed depending on their function in the vaccine.

30

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According to a second aspect of the invention there is provided a computer conditioned to receive information characterising a peptide bound to the MHC molecule and to utilise said information to perform a procedure having the following steps;

- 1) ascertaining the characteristics of a MHC molecule binding groove;
- 2) presenting a selected peptide, which is selected by a predetermined program, to the MHC molecule and ascertaining a first conformation score;
- 3) amending the conformation of the peptide, by way of a predetermined program, and ascertaining a second conformation score;
- 4) repeating step 3 with other conformations of the peptide;
- 5) selecting the peptide conformation with the highest conformation score; and
- 6) calculating the binding score from the conformation score.

Preferably the above detailed procedure also includes a step (7) which comprises repeating steps 1-4 with other peptide fragments in the protein to generate information on all peptide fragments in a protein so that a comparison can be made of the strength of the binding between the peptide and the MHC molecule.

Conveniently the above detailed procedure further comprising a step (8) which comprises altering the conformation of the backbone of the peptide fragment.

The use of a computer in such a task is important because there are hundreds of calculations to perform per peptide fragment. A computer conditioned to perform the task can systematically change the conformation of the side chains and the backbone of the peptide fragment while calculating the conformation score and the binding score.

According to a third aspect of the invention there is provided

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a pharmaceutical composition made by determining the binding affinity of a peptide for a MHC class II molecule.

5 A pharmaceutical composition is thus engineered to contain a peptide which is presented by an MHC class II molecule and which therefore stimulates the bodies cellular immune system. Alternatively the pharmaceutical composition is engineered so that it does not include peptides which significantly stimulate the immune system.

10

The invention will now be described, by way of illustration only, with reference to the following examples, tables and figures accompanying the specification.

15 Figure 1 shows a graphical representation of the binding score distribution of all 554 13-mer Influenza haemagglutinin peptides bound to HLA-DRB1*0101.

Figure 2 shows a graphical representation of the binding score
20 distribution of all 554 13-mer Influenza haemagglutinin peptides bound to HLA-DRB1*0401.

Table 1 shows the value for all the factors required to determine the binding score for the 15 peptides from Influenza
25 haemagglutinin which have the highest binding affinity for HLA-DRB1*0101.

Table 2 shows the value for all the factors required to determine the binding score for the 15 peptides from Influenza
30 haemagglutinin which have the highest binding affinity for HLA-DRB1*0401.

Table 3 lists the sequence difference between HLA-DRB1*0101 and HLA-DRB1*0401.

35

Table 4 shows the torsion angles of the mutated side chains in HLA-DRB1*0401.

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Example 1

The following method was used to confirm that the peptide PKYVKQNTLKLAT, has a high affinity binding for the MHC molecule HLA-DRB1*0101.

- 5 The conformation score was calculated as follows for an oligomeric peptide having thirteen amino acid residues, herein known as a 13-mer peptide:
- a) Calculate the steric overlap between the pocket bound
10 peptide residue in the binding groove and an atom forming the pocket; this is value B.
- b) Count the number of hydrogen bonds which could be formed
15 between the pocket bound peptide residue and atoms forming the pocket; this is value C.
- c) Calculate the strength of electrostatic interactions
20 between any polar atoms of the pocket bound peptide residue and any polar atoms forming the pocket; this is value D.
- d) Count the number of favourable contacts between the pocket
bound peptide residue and atoms forming the pocket; this is
value E.
- 25 These values were then transformed into a conformation score (Z) by using the following equation:

$$Z_n = (cK_2C) - (cK_3D) + (cK_4E) - (cK_1B)$$

where cK_1 to cK_4 are constants and n is the number of the
30 pocket. cK_1 , cK_2 , cK_3 and cK_4 are equal to 100, 1500, 500 and 1000 respectively.

The conformation of each rotatable side chain of the pocket
bound peptide bound residue was then altered by 30° and the
35 conformation score was recalculated.

The above steps were repeated for each of the pockets and the

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highest conformation score for each of the pockets was used to determine the binding score.

The binding score was determined by establishing values for
5 the following parameters:

a) the number of groove-bound hydrophobic residues; this is value F.

b) the number of non groove-bound hydrophilic residues; this is value G.

10 c) the number of peptide residues deemed to fit within their respective binding groove; this is value H.

The conformational scores for pockets one and five were doubled and then all the conformational scores were summed to
15 give a value J.

The above values were then imported in to the following equation in order to determine the binding score:

20
$$J * F^2 * (G * H + 1) + P$$

The binding scores for all the 13-mer peptides from Influenza Haemagglutinin binding with MHC molecule HLA-DRB1*0401 were calculated and the resultant top 15 binding scores are
25 presented in Table 1. PKYVKQNTLKLAT has the 8th highest binding affinity for HLA-DRB1*0101 from all 554 possible overlapping 13-mer peptides.

Table 1

| | Rank | Seq. | Peptide | Binding Score | P | B | C | D | E | F | G | H |
|----|------|------|---------------|---------------|-------|------|---|-------|----|---|---|---|
| 5 | 1 | 328 | NTLKLATGMRNVP | 9382500 | 15012 | 0.00 | 1 | | 27 | 4 | 6 | 5 |
| | 2 | 453 | IDLTDSEMKNLFE | 8288922 | 17964 | 0.72 | 1 | | 40 | 3 | 6 | 5 |
| | 3 | 373 | NSEGTGQAADLKS | 7520420 | 10661 | 0.68 | 0 | +0.01 | 30 | 4 | 7 | |
| | 4 | 504 | HDVYRDEALNNRF | 7211042 | 15527 | 0.56 | 1 | -0.05 | 31 | 3 | 6 | 5 |
| | 5 | 119 | PDYASLRSLVASS | 7174962 | 17351 | 0.68 | 1 | | 40 | 4 | 4 | 5 |
| 10 | 6 | 461 | NKLFEKTRRQLRE | 7049469 | 19407 | 0.79 | 0 | +0.01 | 56 | 2 | 7 | 5 |
| | 7 | 122 | ASLRSLVASSGTL | 6922064 | 16346 | 0.09 | 0 | | 25 | 4 | 4 | 5 |
| | 8 | 322 | PKYVKQNTLKLAT | 6765975 | 18217 | 1.82 | 1 | | 56 | 3 | 5 | 5 |
| | 9 | 458 | SEMKNLFEKTRRQ | 6156822 | 16617 | 0.30 | 4 | +0.08 | 44 | 2 | 7 | 5 |
| | 10 | 513 | NNRFQIKGVELKS | 6096900 | 14052 | 1.32 | 3 | -0.01 | 30 | 4 | 7 | 4 |
| 15 | 11 | 439 | YNAELLVALENQH | 5890199 | 14198 | 0.60 | 1 | | 33 | 4 | 4 | 5 |
| | 12 | 63 | STGKICNNPHRIL | 5887908 | 12776 | 0.75 | 5 | -0.05 | 31 | 3 | 6 | 5 |
| | 13 | 50 | IEVTNATELVQSS | 5503551 | 14297 | 0.95 | 2 | +0.06 | 39 | 3 | 5 | 5 |
| | 14 | 262 | NSNGNLIAPRGYF | 5284475 | 10102 | 0.09 | 1 | | 21 | 4 | 5 | 5 |
| | 15 | 257 | DVLVINSNGNLIA | 5239292 | 17028 | 1.35 | 2 | | 35 | 3 | 4 | 5 |

20

Example 2

A method as described in Example 1 was used to confirm that the peptide PDYASLRSLVASS from Influenza haemagglutinin, has high affinity binding for the MHC molecule HLA-DRB1*0401.

The structure of HLA-DRB1*0401 is not known but a three dimensional model was constructed based on the known structure of HLA-DRB1*0101 by homology modelling. 10 amino acid differences between the two molecules were identified (see Table 2) and HLA-DRB1*0101 was mutated using the molecular modelling package 'Quanta' to produce a model of HLA-DRB1*0401.

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Then the side-chain conformations of the 10 amino acids were adjusted interactively. In most cases, torsion angles were chosen which resulted in little or no steric overlap between the mutated residues and surrounding atoms. In the case of 5 non-conserved residues which were either charged or whose side-chains were able to form hydrogen bonds, the potential to form favourable interactions was also considered. The placement of 13H, 28D and 71K was such that these residues were able to form a favourable electrostatic arrangement 10 whilst at the same time, having minimum steric overlap with surrounding atoms. In the case of 30Y, this residue was positioned such that its hydroxyl group was situated close to the side-chain of 9E, where a hydrogen bond may be formed. The torsion angles chosen for the 10 mutated amino acid 15 residues were calculated in accordance with the standard conventions and are listed in Table 3.

The binding scores for all 13-mer peptides from Influenza Haemagglutinin binding with MHC molecule HLA-DRB1*0401 were 20 calculated and the resultant top 15 binding scores are presented in Table 4. PDYASLRSLVASS has the 9th highest binding affinity for HLA-DRB1*0401 from all 554 possible overlapping 13-mer peptides.

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Table 2

| Seq. Pos. | HLA-DRB1*0101 | HLA-DRB1*0401 |
|-----------|---------------|---------------|
| b9 | Tryptophan | Glutamic acid |
| b11 | Leucine | Valine |
| 5 b13 | Phenylalanine | Histidine |
| b26 | Leucine | Phenylalanine |
| b28 | Glutamic acid | Aspartic Acid |
| b30 | Cysteine | Tyrosine |
| b31 | Isoleucine | Phenylalanine |
| 10 b33 | Asparagine | Histidine |
| b37 | Serine | Tyrosine |
| b71 | Arginine | Lysine |

Table 3

15

| Residue | c1 | c2 | c3 | c4 |
|---------|-------|------|------|----|
| b9 | -61° | -71° | -2° | |
| b11 | 168° | | | |
| b13 | -38° | -63° | | |
| 20 b26 | 170° | 57° | | |
| b28 | -174° | -15° | | |
| b30 | -174° | 41° | | |
| b31 | -119° | -13° | | |
| b33 | -95° | -2° | | |
| 25 b37 | -116° | -2° | | |
| b71 | -97° | -45° | 172° | 9° |

Table 4

| Rank | Seq. | Peptide | Binding Score | P | B | C | D | E | F | G | H |
|------|------|----------------|------------------|------|------|---|-------|----|---|---|---|
| 1 | 453 | IDLTDSEMKNLFE | 3070823 | 6559 | 0.36 | 0 | | 42 | 3 | 6 | 5 |
| 2 | 373 | NSEGTGQAADLKS | 2988447 | 4182 | 0.36 | 0 | +0.01 | 32 | 4 | 7 | 5 |
| 3 | 328 | NTLKLATGMRNVP | 2899375 | 4639 | 0.00 | 1 | | 27 | 4 | 6 | 5 |
| 4 | 122 | ASLRSLVASSGTL | 2894599 | 6819 | 0.03 | 0 | | 24 | 4 | 4 | 5 |
| 5 | 72 | HRILDGIDCTLID | 2820446 | 4623 | 0.60 | 1 | +0.16 | 28 | 4 | 6 | 5 |
| 6 | 461 | NKLF EKTRRQLRE | 2662369 | 7203 | 0.36 | 0 | -0.11 | 50 | 2 | 7 | 5 |
| 7 | 119 | PDYASLRSLVASS | 2616648 | 6184 | 0.11 | 1 | | 32 | 4 | 4 | 5 |
| 8 | 188 | DNFDKLYIWGIHH | 2615259 | 5429 | 0.58 | 0 | | 29 | 5 | 6 | 4 |
| 9 | 322 | PKYVKQNTLKLAT | 2515861 | 6407 | 0.46 | 2 | | 44 | 3 | 5 | 5 |
| 10 | 232 | NIGSRPWVRLSS | 2488137 | 4818 | 0.41 | 0 | -0.02 | 35 | 4 | 5 | 5 |
| 11 | 504 | HDVYRDEALNNRF | 2353661 | 4965 | 0.05 | 1 | -0.07 | 25 | 3 | 6 | 5 |
| 12 | 135 | EFITEGFTWTGVT | 2208179 | 3543 | 0.07 | 1 | | 20 | 4 | 5 | 5 |
| 13 | 251 | TIVKPGDVLVINS | 2176819 | 5259 | 0.10 | 0 | | 16 | 5 | 5 | 4 |
| 14 | 257 | DVLVINSNGNLIA | 2107570 | 6673 | 0.71 | 2 | | 40 | 3 | 4 | 5 |
| 15 | 439 | YNAELLVALENQH | 2035430 | 4795 | 0.03 | 1 | | 26 | 4 | 4 | 5 |

20 Example 3

A library of backbones were constructed by examining the crystal structure of the HLA-DR1 complexed with SEB super-antigen. This results in a collection of homogenous peptides within the MHC binding groove. The atomic positions of the peptide backbone, as shown in the PDB file produced from the crystal, were considered to be the 'representative' backbone conformation of a peptide which binds to HLA-DR1.

Each of the peptide backbone conformations from the known MHC class II crystallographic structures are taken and after being transformed to the same frame of reference as the 'representative' peptide had the differences between their C α /C β positions and those of the 'representative' peptide

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calculated. These differences summarise the variability of $C\alpha/C\beta$ atomic positions between the known peptides and the 'representative' peptide.

- 5 The differences were doubled to take into account the fact that the variability of peptides thus far crystallised may not fully represent the true variability of peptides binding to MHC class II molecules. The differences were then used to define regions within which peptide $C\alpha$ and $C\beta$ atoms centres
10 are constrained to lie.

An exhaustive search was then made through candidate peptide backbones. Starting from the 'representative' peptide candidates are generated by adjusting backbone ϕ and ψ angles
15 in ten degree steps from the N-terminus to the C-terminus. An adjustment was rejected if it led to any $C\alpha$ or $C\beta$ atom centre being outside the allowed region, derived above. An adjustment which did not violate the constraint results in a new backbone conformation which is stored within the peptide
20 backbone library.

The x, y, and z co-ordinates of atoms in the backbones designated 0, 14, 62, 65, 75, 93, 104, 107, 112, 118, 129, 134, 141, 144 are given in Tables 5 to 18.

Table 5

| Backbone 0 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 19.913 | 86.191 | 20.687 |
| 1 | CA | 0 | 19.472 | 86.222 | 22.078 |
| 2 | C | 0 | 18.153 | 85.531 | 22.516 |
| 3 | O | 0 | 18.200 | 84.640 | 23.352 |
| 4 | CB | 0 | 19.504 | 87.660 | 22.593 |
| 5 | N | 1 | 16.984 | 85.957 | 22.044 |
| 6 | CA | 1 | 15.771 | 85.316 | 22.536 |
| 7 | C | 1 | 15.262 | 84.115 | 21.770 |
| 8 | O | 1 | 15.175 | 84.127 | 20.547 |
| 9 | CB | 1 | 14.663 | 86.325 | 22.743 |
| 10 | N | 2 | 14.959 | 83.055 | 22.510 |
| 11 | CA | 2 | 14.414 | 81.829 | 21.926 |
| 12 | C | 2 | 12.920 | 82.131 | 21.907 |
| 13 | O | 2 | 12.384 | 82.737 | 22.840 |
| 14 | CB | 2 | 14.756 | 80.548 | 22.811 |
| 15 | N | 3 | 12.283 | 81.841 | 20.784 |
| 16 | CA | 3 | 10.866 | 82.097 | 20.637 |
| 17 | C | 3 | 10.086 | 80.785 | 20.839 |
| 18 | O | 3 | 10.560 | 79.730 | 20.447 |
| 19 | CB | 3 | 10.624 | 82.744 | 19.230 |
| 20 | N | 4 | 8.951 | 80.855 | 21.528 |
| 21 | CA | 4 | 8.035 | 79.734 | 21.814 |
| 22 | C | 4 | 6.945 | 79.658 | 20.721 |
| 23 | O | 4 | 6.664 | 80.648 | 20.044 |
| 24 | CB | 4 | 7.330 | 79.991 | 23.185 |
| 25 | N | 5 | 6.355 | 78.499 | 20.461 |
| 26 | CA | 5 | 5.266 | 78.527 | 19.496 |
| 27 | C | 5 | 4.167 | 78.292 | 20.475 |
| 28 | O | 5 | 4.342 | 77.560 | 21.444 |
| 29 | CB | 5 | 5.349 | 77.437 | 18.471 |
| 30 | N | 6 | 3.044 | 78.938 | 20.261 |
| 31 | CA | 6 | 1.950 | 78.858 | 21.205 |
| 32 | C | 6 | 1.050 | 77.758 | 20.856 |
| 33 | O | 6 | 0.836 | 77.517 | 19.690 |
| 34 | CB | 6 | 1.163 | 80.226 | 21.247 |
| 35 | N | 7 | 0.420 | 77.190 | 21.863 |
| 36 | CA | 7 | -0.503 | 76.102 | 21.660 |
| 37 | C | 7 | -1.889 | 76.607 | 21.227 |
| 38 | O | 7 | -2.429 | 77.551 | 21.833 |
| 39 | CB | 7 | -0.611 | 75.340 | 22.937 |
| 40 | N | 8 | -2.442 | 75.997 | 20.167 |
| 41 | CA | 8 | -3.790 | 76.330 | 19.644 |

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Table 5 continued

| | Atom Number | Atom type | Position in peptide | x | y | z |
|----|----------------|--------------|------------------------|---------|--------|--------|
| 5 | 42 | C | 8 | -4.839 | 75.618 | 20.504 |
| | 43 | O | 8 | -4.505 | 74.687 | 21.236 |
| | 44 | CB | 8 | -3.924 | 75.908 | 18.149 |
| | 45 | N | 9 | -6.093 | 76.041 | 20.436 |
| | 46 | CA | 9 | -7.113 | 75.382 | 21.236 |
| 10 | 47 | C | 9 | -7.976 | 74.424 | 20.403 |
| | 48 | O | 9 | -8.366 | 74.742 | 19.266 |
| | 49 | CB | 9 | -7.963 | 76.413 | 21.973 |
| | 50 | N | 10 | -8.203 | 73.232 | 20.971 |
| | 51 | CA | 10 | -8.995 | 72.149 | 20.365 |
| | 52 | C | 10 | -10.492 | 72.527 | 20.200 |
| | 53 | O | 10 | -10.962 | 73.563 | 20.702 |
| | 54 | CB | 10 | -8.830 | 70.835 | 21.191 |
| | 55 | N | 11 | -11.238 | 71.661 | 19.523 |
| | 56 | CA | 11 | -12.654 | 71.907 | 19.270 |
| 15 | 57 | C | 11 | -13.603 | 71.483 | 20.395 |
| | 58 | O | 11 | -13.661 | 70.302 | 20.800 |
| | 59 | CB | 11 | -13.072 | 71.269 | 17.940 |
| | 60 | N | 12 | -14.360 | 72.481 | 20.852 |
| | 61 | CA | 12 | -15.363 | 72.337 | 21.898 |
| | 62 | C | 12 | -14.758 | 72.166 | 23.281 |
| | 63 | O | 12 | -14.785 | 71.069 | 23.853 |
| | 64 | CB | 12 | -16.320 | 71.168 | 21.577 |

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Table 6

| Backbone 14 | | | | | | |
|-------------|--------|------|------------|--------|--------|--------|
| 5 | Atom | Atom | Position | x | y | z |
| | Number | type | in peptide | | | |
| | 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| | 1 | CA | 0 | 18.281 | 86.637 | 22.405 |
| | 2 | C | 0 | 16.799 | 86.756 | 22.715 |
| | 3 | O | 0 | 16.250 | 87.880 | 22.720 |
| | 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 10 | 5 | N | 1 | 16.174 | 85.601 | 22.931 |
| | 6 | CA | 1 | 14.768 | 85.553 | 23.287 |
| | 7 | C | 1 | 14.098 | 84.393 | 22.569 |
| | 8 | O | 1 | 13.053 | 84.588 | 21.908 |
| | 9 | CB | 1 | 14.090 | 86.846 | 22.869 |
| | 10 | N | 2 | 14.723 | 83.223 | 22.680 |
| | 11 | CA | 2 | 14.182 | 82.013 | 22.093 |
| | 12 | C | 2 | 12.659 | 82.164 | 21.901 |
| | 13 | O | 2 | 11.952 | 82.431 | 22.884 |
| | 14 | CB | 2 | 14.470 | 80.825 | 22.994 |
| 15 | 15 | N | 3 | 12.242 | 82.022 | 20.649 |
| | 16 | CA | 3 | 10.845 | 82.086 | 20.317 |
| | 17 | C | 3 | 10.219 | 80.681 | 20.423 |
| | 18 | O | 3 | 10.898 | 79.694 | 20.101 |
| | 19 | CB | 3 | 10.669 | 82.621 | 18.906 |
| | 20 | N | 4 | 8.980 | 80.660 | 20.898 |
| | 21 | CA | 4 | 8.245 | 79.430 | 21.010 |
| | 22 | C | 4 | 6.863 | 79.586 | 20.344 |
| | 23 | O | 4 | 6.283 | 80.680 | 20.413 |
| | 24 | CB | 4 | 8.071 | 79.059 | 22.472 |
| 20 | 25 | N | 5 | 6.427 | 78.504 | 19.710 |
| | 26 | CA | 5 | 5.135 | 78.479 | 19.082 |
| | 27 | C | 5 | 4.084 | 77.942 | 20.074 |
| | 28 | O | 5 | 4.171 | 76.770 | 20.468 |
| | 29 | CB | 5 | 5.174 | 77.593 | 17.848 |
| 25 | 30 | N | 6 | 3.174 | 78.832 | 20.452 |
| | 31 | CA | 6 | 2.100 | 78.470 | 21.336 |
| | 32 | C | 6 | 1.349 | 77.248 | 20.769 |
| | 33 | O | 6 | 1.703 | 76.776 | 19.678 |
| | 34 | CB | 6 | 1.139 | 79.635 | 21.492 |
| | 35 | N | 7 | 0.381 | 76.781 | 21.550 |
| | 36 | CA | 7 | -0.441 | 75.677 | 21.137 |
| | 37 | C | 7 | -1.906 | 76.139 | 21.008 |
| | 38 | O | 7 | -2.505 | 76.533 | 22.020 |
| | 39 | CB | 7 | -0.346 | 74.551 | 22.153 |
| 30 | 40 | N | 8 | -2.392 | 76.101 | 19.773 |
| | 41 | CA | 8 | -3.758 | 76.454 | 19.498 |
| | 42 | C | 8 | -4.704 | 75.537 | 20.299 |
| | 43 | O | 8 | -4.316 | 74.404 | 20.618 |
| | 44 | CB | 8 | -4.043 | 76.313 | 18.013 |

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Table 6 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 45 | N | 9 | -5.873 | 76.084 | 20.610 |
| 46 | CA | 9 | -6.881 | 75.338 | 21.313 |
| 47 | C | 9 | -7.500 | 74.285 | 20.371 |
| 48 | O | 9 | -7.243 | 74.336 | 19.159 |
| 49 | CB | 9 | -7.964 | 76.275 | 21.818 |
| 50 | N | 10 | -8.250 | 73.372 | 20.978 |
| 51 | CA | 10 | -8.934 | 72.354 | 20.229 |
| 52 | C | 10 | -10.393 | 72.786 | 19.976 |
| 53 | O | 10 | -11.075 | 73.192 | 20.928 |
| 54 | CB | 10 | -8.914 | 71.043 | 20.996 |
| 55 | N | 11 | -10.781 | 72.710 | 18.708 |
| 56 | CA | 11 | -12.127 | 73.032 | 18.320 |
| 57 | C | 11 | -13.058 | 71.846 | 18.640 |
| 58 | O | 11 | -13.254 | 70.984 | 17.770 |
| 59 | CB | 11 | -12.180 | 73.341 | 16.834 |
| 60 | N | 12 | -13.551 | 71.844 | 19.872 |
| 61 | CA | 12 | -14.474 | 70.830 | 20.305 |
| 62 | C | 12 | 0.000 | -12.127 | 73.032 |
| 63 | O | 12 | 18.356 | 0.000 | -12.127 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

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Table 7

| Backbone 62 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.315 | 86.971 | 22.396 |
| 2 | C | 0 | 16.796 | 86.979 | 22.404 |
| 3 | O | 0 | 16.173 | 87.867 | 21.780 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.231 | 85.979 | 23.075 |
| 6 | CA | 1 | 14.791 | 85.876 | 23.216 |
| 7 | C | 1 | 14.286 | 84.665 | 22.451 |
| 8 | O | 1 | 13.659 | 84.820 | 21.380 |
| 9 | CB | 1 | 14.132 | 87.123 | 22.652 |
| 10 | N | 2 | 14.595 | 83.487 | 22.989 |
| 11 | CA | 2 | 14.144 | 82.241 | 22.404 |
| 12 | C | 2 | 12.614 | 82.280 | 22.212 |
| 13 | O | 2 | 11.890 | 82.495 | 23.195 |
| 14 | CB | 2 | 14.518 | 81.077 | 23.305 |
| 15 | N | 3 | 12.208 | 82.108 | 20.960 |
| 16 | CA | 3 | 10.810 | 82.071 | 20.629 |
| 17 | C | 3 | 10.289 | 80.623 | 20.734 |
| 18 | O | 3 | 11.105 | 79.691 | 20.783 |
| 19 | CB | 3 | 10.596 | 82.591 | 19.218 |
| 20 | N | 4 | 8.967 | 80.514 | 20.800 |
| 21 | CA | 4 | 8.328 | 79.228 | 20.852 |
| 22 | C | 4 | 6.861 | 79.356 | 20.395 |
| 23 | O | 4 | 6.157 | 80.256 | 20.876 |
| 24 | CB | 4 | 8.377 | 78.680 | 22.268 |
| 25 | N | 5 | 6.490 | 78.478 | 19.470 |
| 26 | CA | 5 | 5.140 | 78.440 | 18.978 |
| 27 | C | 5 | 4.171 | 78.141 | 20.139 |
| 28 | O | 5 | 4.543 | 77.392 | 21.055 |
| 29 | CB | 5 | 5.006 | 77.369 | 17.909 |
| 30 | N | 6 | 3.002 | 78.765 | 20.060 |
| 31 | CA | 6 | 1.975 | 78.549 | 21.042 |
| 32 | C | 6 | 1.039 | 77.416 | 20.577 |
| 33 | O | 6 | 1.276 | 76.842 | 19.503 |
| 34 | CB | 6 | 1.174 | 79.824 | 21.246 |
| 35 | N | 7 | 0.052 | 77.131 | 21.418 |
| 36 | CA | 7 | -0.931 | 76.132 | 21.102 |
| 37 | C | 7 | -2.325 | 76.784 | 21.008 |
| 38 | O | 7 | -2.553 | 77.814 | 21.661 |
| 39 | CB | 7 | -0.941 | 75.055 | 22.174 |
| 40 | N | 8 | -3.166 | 76.177 | 20.179 |
| 41 | CA | 8 | -4.518 | 76.638 | 20.020 |
| 42 | C | 8 | -5.491 | 75.631 | 20.666 |
| 43 | O | 8 | -5.155 | 74.441 | 20.754 |

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Table 7 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 44 | CB | 8 | -4.845 | 76.793 | 18.545 |
| 45 | N | 9 | -6.623 | 76.163 | 21.113 |
| 46 | CA | 9 | -7.650 | 75.345 | 21.696 |
| 47 | C | 9 | -8.161 | 74.329 | 20.655 |
| 48 | O | 9 | -8.197 | 74.658 | 19.460 |
| 49 | CB | 9 | -8.802 | 76.215 | 22.170 |
| 50 | N | 10 | -8.492 | 73.143 | 21.153 |
| 51 | CA | 10 | -9.030 | 72.107 | 20.315 |
| 52 | C | 10 | -10.518 | 72.390 | 20.029 |
| 53 | O | 10 | -11.258 | 72.730 | 20.964 |
| 54 | CB | 10 | -8.887 | 70.758 | 21.000 |
| 55 | N | 11 | -10.869 | 72.271 | 18.754 |
| 56 | CA | 11 | -12.232 | 72.455 | 18.336 |
| 57 | C | 11 | -13.047 | 71.182 | 18.641 |
| 58 | O | 11 | -13.155 | 70.312 | 17.764 |
| 59 | CB | 11 | -12.284 | 72.752 | 16.847 |
| 60 | N | 12 | -13.544 | 71.124 | 19.871 |
| 61 | CA | 12 | -14.366 | 70.022 | 20.291 |
| 62 | C | 12 | 0.000 | -12.232 | 72.455 |
| 63 | O | 12 | 18.332 | 0.000 | -12.232 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

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Table 8

| Backbone 65 | | | | | |
|-------------|-----------|---------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.487 | 86.641 | 22.418 |
| 2 | C | 0 | 16.990 | 86.870 | 22.533 |
| 3 | O | 0 | 16.510 | 87.999 | 22.287 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.279 | 85.796 | 22.868 |
| 6 | CA | 1 | 14.844 | 85.866 | 23.065 |
| 7 | C | 1 | 14.178 | 84.664 | 22.417 |
| 8 | O | 1 | 13.234 | 84.830 | 21.612 |
| 9 | CB | 1 | 14.301 | 87.132 | 22.424 |
| 10 | N | 2 | 14.699 | 83.484 | 22.746 |
| 11 | CA | 2 | 14.144 | 82.241 | 22.248 |
| 12 | C | 2 | 12.616 | 82.381 | 22.089 |
| 13 | O | 2 | 11.950 | 82.822 | 23.038 |
| 14 | CB | 2 | 14.457 | 81.109 | 23.212 |
| 15 | N | 3 | 12.150 | 82.035 | 20.895 |
| 16 | CA | 3 | 10.742 | 82.065 | 20.608 |
| 17 | C | 3 | 10.206 | 80.624 | 20.484 |
| 18 | O | 3 | 10.895 | 79.773 | 19.902 |
| 19 | CB | 3 | 10.491 | 82.818 | 19.314 |
| 20 | N | 4 | 9.029 | 80.419 | 21.065 |
| 21 | CA | 4 | 8.376 | 79.140 | 20.993 |
| 22 | C | 4 | 6.930 | 79.322 | 20.491 |
| 23 | O | 4 | 6.309 | 80.350 | 20.801 |
| 24 | CB | 4 | 8.365 | 78.486 | 22.364 |
| 25 | N | 5 | 6.484 | 78.339 | 19.718 |
| 26 | CA | 5 | 5.139 | 78.340 | 19.212 |
| 27 | C | 5 | 4.150 | 78.069 | 20.363 |
| 28 | O | 5 | 4.487 | 77.306 | 21.280 |
| 29 | CB | 5 | 4.985 | 77.274 | 18.142 |
| 30 | N | 6 | 3.002 | 78.731 | 20.275 |
| 31 | CA | 6 | 1.959 | 78.547 | 21.246 |
| 32 | C | 6 | 0.861 | 77.634 | 20.665 |
| 33 | O | 6 | 0.752 | 77.533 | 19.433 |
| 34 | CB | 6 | 1.360 | 79.890 | 21.628 |
| 35 | N | 7 | 0.134 | 76.994 | 21.573 |
| 36 | CA | 7 | -0.959 | 76.143 | 21.187 |
| 37 | C | 7 | -1.983 | 76.952 | 20.366 |
| 38 | O | 7 | -1.708 | 78.116 | 20.039 |
| 39 | CB | 7 | -1.631 | 75.569 | 22.422 |
| 40 | N | 8 | -3.087 | 76.287 | 20.048 |
| 41 | CA | 8 | -4.156 | 76.921 | 19.326 |
| 42 | C | 8 | -5.496 | 76.242 | 19.676 |

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Table 8 continued

| | Atom Number | Atom type | Position in peptide | x | y | z |
|----|----------------|--------------|------------------------|---------|---------|---------|
| 5 | 43 | O | 8 | -6.146 | 75.692 | 18.775 |
| | 44 | CB | 8 | -3.906 | 76.820 | 17.831 |
| | 45 | N | 9 | -5.817 | 76.283 | 20.964 |
| | 46 | CA | 9 | -7.058 | 75.736 | 21.439 |
| | 47 | C | 9 | -7.606 | 74.721 | 20.416 |
| | 48 | O | 9 | -7.311 | 74.855 | 19.219 |
| | 49 | CB | 9 | -8.071 | 76.849 | 21.649 |
| | 50 | N | 10 | -8.339 | 73.746 | 20.940 |
| 10 | 51 | CA | 10 | -8.959 | 72.751 | 20.108 |
| | 52 | C | 10 | -10.421 | 73.147 | 19.824 |
| | 53 | O | 10 | -10.685 | 73.773 | 18.787 |
| | 54 | CB | 10 | -8.919 | 71.398 | 20.799 |
| | 55 | N | 11 | -11.294 | 72.734 | 20.735 |
| | 56 | CA | 11 | -12.689 | 73.067 | 20.635 |
| | 57 | C | 11 | -13.474 | 71.860 | 20.085 |
| | 58 | O | 11 | -13.031 | 71.253 | 19.099 |
| 15 | 59 | CB | 11 | -12.873 | 74.262 | 19.715 |
| | 60 | N | 12 | -14.572 | 71.556 | 20.766 |
| | 61 | CA | 12 | -15.436 | 70.486 | 20.348 |
| | 62 | C | 12 | 0.000 | -12.689 | 73.067 |
| | 63 | O | 12 | 18.675 | 0.000 | -12.689 |
| | 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

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Table 9

| Backbone 75 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.442 | 86.539 | 22.377 |
| 2 | C | 0 | 16.947 | 86.419 | 22.136 |
| 3 | O | 0 | 16.452 | 86.839 | 21.066 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.265 | 85.822 | 23.109 |
| 6 | CA | 1 | 14.823 | 85.676 | 23.048 |
| 7 | C | 1 | 14.466 | 84.417 | 22.277 |
| 8 | O | 1 | 14.197 | 84.487 | 21.057 |
| 9 | CB | 1 | 14.218 | 86.875 | 22.338 |
| 10 | N | 2 | 14.505 | 83.290 | 22.985 |
| 11 | CA | 2 | 14.144 | 82.013 | 22.404 |
| 12 | C | 2 | 12.615 | 81.942 | 22.214 |
| 13 | O | 2 | 11.895 | 81.727 | 23.200 |
| 14 | CB | 2 | 14.601 | 80.882 | 23.308 |
| 15 | N | 3 | 12.201 | 82.159 | 20.971 |
| 16 | CA | 3 | 10.808 | 82.078 | 20.626 |
| 17 | C | 3 | 10.331 | 80.615 | 20.726 |
| 18 | O | 3 | 11.176 | 79.709 | 20.772 |
| 19 | CB | 3 | 10.592 | 82.592 | 19.213 |
| 20 | N | 4 | 9.013 | 80.465 | 20.789 |
| 21 | CA | 4 | 8.414 | 79.160 | 20.836 |
| 22 | C | 4 | 6.944 | 79.245 | 20.377 |
| 23 | O | 4 | 6.322 | 80.304 | 20.544 |
| 24 | CB | 4 | 8.478 | 78.609 | 22.251 |
| 25 | N | 5 | 6.482 | 78.145 | 19.793 |
| 26 | CA | 5 | 5.116 | 78.053 | 19.354 |
| 27 | C | 5 | 4.181 | 77.969 | 20.577 |
| 28 | O | 5 | 4.609 | 77.470 | 21.629 |
| 29 | CB | 5 | 4.932 | 76.823 | 18.483 |
| 30 | N | 6 | 2.974 | 78.490 | 20.389 |
| 31 | CA | 6 | 1.974 | 78.445 | 21.420 |
| 32 | C | 6 | 0.736 | 77.679 | 20.910 |
| 33 | O | 6 | 0.349 | 77.867 | 19.748 |
| 34 | CB | 6 | 1.576 | 79.855 | 21.821 |
| 35 | N | 7 | 0.206 | 76.836 | 21.788 |
| 36 | CA | 7 | -0.980 | 76.086 | 21.478 |
| 37 | C | 7 | -1.844 | 76.872 | 20.470 |
| 38 | O | 7 | -1.448 | 77.977 | 20.071 |
| 39 | CB | 7 | -1.778 | 75.828 | 22.745 |
| 40 | N | 8 | -2.952 | 76.249 | 20.088 |
| 41 | CA | 8 | -3.885 | 76.873 | 19.189 |

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Table 9 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 42 | C | 8 | -5.324 | 76.483 | 19.579 |
| 43 | O | 8 | -6.195 | 76.435 | 18.698 |
| 44 | CB | 8 | -3.604 | 76.435 | 17.762 |
| 45 | N | 9 | -5.491 | 76.194 | 20.865 |
| 46 | CA | 9 | -6.786 | 75.859 | 21.391 |
| 47 | C | 9 | -7.424 | 74.747 | 20.535 |
| 48 | O | 9 | -7.209 | 74.729 | 19.314 |
| 49 | CB | 9 | -7.681 | 77.087 | 21.388 |
| 50 | N | 10 | -8.142 | 73.864 | 21.219 |
| 51 | CA | 10 | -8.840 | 72.797 | 20.556 |
| 52 | C | 10 | -10.312 | 73.196 | 20.334 |
| 53 | O | 10 | -10.616 | 73.833 | 19.314 |
| 54 | CB | 10 | -8.772 | 71.532 | 21.394 |
| 55 | N | 11 | -11.149 | 72.774 | 21.275 |
| 56 | CA | 11 | -12.546 | 73.108 | 21.233 |
| 57 | C | 11 | -13.321 | 72.011 | 20.475 |
| 58 | O | 11 | -12.815 | 71.509 | 19.460 |
| 59 | CB | 11 | -12.741 | 74.445 | 20.540 |
| 60 | N | 12 | -14.483 | 71.674 | 21.023 |
| 61 | CA | 12 | -15.343 | 70.702 | 20.406 |
| 62 | C | 12 | 0.000 | -12.546 | 73.108 |
| 63 | O | 12 | 18.817 | 0.000 | -12.546 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

Table 10

| Backbone 93 | | | | | |
|-------------|-----------|---------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.249 | 86.312 | 21.629 |
| 2 | C | 0 | 16.910 | 86.341 | 22.345 |
| 3 | O | 0 | 16.646 | 87.271 | 23.139 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.080 | 85.351 | 22.027 |
| 6 | CA | 1 | 14.782 | 85.213 | 22.662 |
| 7 | C | 1 | 14.078 | 83.978 | 22.127 |
| 8 | O | 1 | 12.999 | 84.095 | 21.505 |
| 9 | CB | 1 | 13.932 | 86.434 | 22.357 |
| 10 | N | 2 | 14.712 | 82.828 | 22.345 |
| 11 | CA | 2 | 14.144 | 81.558 | 21.938 |
| 12 | C | 2 | 12.613 | 81.689 | 21.812 |
| 13 | O | 2 | 11.912 | 81.568 | 22.828 |
| 14 | CB | 2 | 14.484 | 80.486 | 22.959 |
| 15 | N | 3 | 12.179 | 81.964 | 20.587 |
| 16 | CA | 3 | 10.775 | 82.068 | 20.300 |
| 17 | C | 3 | 10.163 | 80.658 | 20.176 |
| 18 | O | 3 | 10.712 | 79.826 | 19.439 |
| 19 | CB | 3 | 10.564 | 82.834 | 19.005 |
| 20 | N | 4 | 9.085 | 80.454 | 20.925 |
| 21 | CA | 4 | 8.374 | 79.206 | 20.882 |
| 22 | C | 4 | 7.026 | 79.401 | 20.159 |
| 23 | O | 4 | 6.568 | 80.546 | 20.036 |
| 24 | CB | 4 | 8.130 | 78.697 | 22.292 |
| 25 | N | 5 | 6.482 | 78.283 | 19.690 |
| 26 | CA | 5 | 5.203 | 78.295 | 19.035 |
| 27 | C | 5 | 4.087 | 78.033 | 20.066 |
| 28 | O | 5 | 4.298 | 77.235 | 20.991 |
| 29 | CB | 5 | 5.163 | 77.229 | 17.954 |
| 30 | N | 6 | 2.980 | 78.741 | 19.876 |
| 31 | CA | 6 | 1.833 | 78.572 | 20.726 |
| 32 | C | 6 | 1.164 | 77.213 | 20.434 |
| 33 | O | 6 | 1.603 | 76.513 | 19.510 |
| 34 | CB | 6 | 0.839 | 79.695 | 20.486 |
| 35 | N | 7 | 0.169 | 76.899 | 21.254 |
| 36 | CA | 7 | -0.585 | 75.687 | 21.080 |
| 37 | C | 7 | -2.092 | 76.013 | 21.037 |
| 38 | O | 7 | -2.667 | 76.338 | 22.086 |
| 39 | CB | 7 | -0.300 | 74.729 | 22.223 |
| 40 | N | 8 | -2.639 | 75.944 | 19.829 |
| 41 | CA | 8 | -4.045 | 76.173 | 19.635 |
| 42 | C | 8 | -4.853 | 75.344 | 20.653 |
| 43 | O | 8 | -4.314 | 74.368 | 21.198 |

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Table 10 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 44 | CB | 8 | -4.445 | 75.782 | 18.223 |
| 45 | N | 9 | -6.082 | 75.791 | 20.882 |
| 46 | CA | 9 | -6.974 | 75.097 | 21.769 |
| 47 | C | 9 | -8.018 | 74.312 | 20.948 |
| 48 | O | 9 | -8.754 | 74.928 | 20.163 |
| 49 | CB | 9 | -7.679 | 76.089 | 22.679 |
| 50 | N | 10 | -8.002 | 72.999 | 21.144 |
| 51 | CA | 10 | -8.947 | 72.137 | 20.488 |
| 52 | C | 10 | -10.274 | 72.891 | 20.269 |
| 53 | O | 10 | -10.348 | 73.727 | 19.356 |
| 54 | CB | 10 | -9.194 | 70.899 | 21.332 |
| 55 | N | 11 | -11.256 | 72.533 | 21.087 |
| 56 | CA | 11 | -12.539 | 73.179 | 21.038 |
| 57 | C | 11 | -13.542 | 72.288 | 20.278 |
| 58 | O | 11 | -13.224 | 71.836 | 19.167 |
| 59 | CB | 11 | -12.418 | 74.524 | 20.343 |
| 60 | N | 12 | -14.678 | 72.054 | 20.925 |
| 61 | CA | 12 | -15.731 | 71.281 | 20.326 |
| 62 | C | 12 | 0.000 | -12.539 | 73.179 |
| 63 | O | 12 | 18.616 | 0.000 | -12.539 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

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Table 11

| Backbone 104 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.400 | 86.585 | 22.355 |
| 2 | C | 0 | 16.914 | 86.850 | 22.523 |
| 3 | O | 0 | 16.453 | 87.991 | 22.296 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.189 | 85.793 | 22.880 |
| 6 | CA | 1 | 14.763 | 85.897 | 23.128 |
| 7 | C | 1 | 14.059 | 84.662 | 22.593 |
| 8 | O | 1 | 12.980 | 84.778 | 21.971 |
| 9 | CB | 1 | 14.210 | 87.122 | 22.421 |
| 10 | N | 2 | 14.693 | 83.511 | 22.810 |
| 11 | CA | 2 | 14.125 | 82.241 | 22.404 |
| 12 | C | 2 | 12.594 | 82.372 | 22.277 |
| 13 | O | 2 | 11.945 | 82.807 | 23.241 |
| 14 | CB | 2 | 14.465 | 81.169 | 23.424 |
| 15 | N | 3 | 12.104 | 82.026 | 21.093 |
| 16 | CA | 3 | 10.690 | 82.048 | 20.837 |
| 17 | C | 3 | 10.159 | 80.604 | 20.723 |
| 18 | O | 3 | 10.919 | 79.713 | 20.317 |
| 19 | CB | 3 | 10.406 | 82.801 | 19.548 |
| 20 | N | 4 | 8.902 | 80.444 | 21.120 |
| 21 | CA | 4 | 8.250 | 79.166 | 21.029 |
| 22 | C | 4 | 6.905 | 79.319 | 20.290 |
| 23 | O | 4 | 6.415 | 80.450 | 20.160 |
| 24 | CB | 4 | 8.009 | 78.605 | 22.420 |
| 25 | N | 5 | 6.401 | 78.185 | 19.817 |
| 26 | CA | 5 | 5.130 | 78.158 | 19.147 |
| 27 | C | 5 | 4.011 | 77.862 | 20.165 |
| 28 | O | 5 | 4.164 | 76.935 | 20.975 |
| 29 | CB | 5 | 5.135 | 77.091 | 18.066 |
| 30 | N | 6 | 2.968 | 78.680 | 20.096 |
| 31 | CA | 6 | 1.823 | 78.502 | 20.947 |
| 32 | C | 6 | 1.166 | 77.138 | 20.656 |
| 33 | O | 6 | 1.718 | 76.360 | 19.864 |
| 34 | CB | 6 | 0.819 | 79.617 | 20.708 |
| 35 | N | 7 | 0.047 | 76.906 | 21.334 |
| 36 | CA | 7 | -0.707 | 75.699 | 21.135 |
| 37 | C | 7 | -2.213 | 76.030 | 21.083 |
| 38 | O | 7 | -2.793 | 76.357 | 22.129 |
| 39 | CB | 7 | -0.435 | 74.724 | 22.267 |
| 40 | N | 8 | -2.754 | 75.961 | 19.873 |
| 41 | CA | 8 | -4.157 | 76.194 | 19.670 |
| 42 | C | 8 | -4.974 | 75.368 | 20.684 |
| 43 | O | 8 | -4.444 | 74.387 | 21.228 |

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Table 11 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 44 | CB | 8 | -4.550 | 75.803 | 18.256 |
| 45 | N | 9 | -6.200 | 75.824 | 20.911 |
| 46 | CA | 9 | -7.100 | 75.134 | 21.794 |
| 47 | C | 9 | -8.146 | 74.358 | 20.969 |
| 48 | O | 9 | -8.997 | 74.991 | 20.328 |
| 49 | CB | 9 | -7.800 | 76.129 | 22.704 |
| 50 | N | 10 | -8.007 | 73.038 | 21.000 |
| 51 | CA | 10 | -8.934 | 72.175 | 20.320 |
| 52 | C | 10 | -10.266 | 72.919 | 20.092 |
| 53 | O | 10 | -10.341 | 73.752 | 19.177 |
| 54 | CB | 10 | -9.181 | 70.924 | 21.145 |
| 55 | N | 11 | -11.249 | 72.557 | 20.907 |
| 56 | CA | 11 | -12.537 | 73.194 | 20.850 |
| 57 | C | 11 | -13.529 | 72.294 | 20.086 |
| 58 | O | 11 | -13.514 | 72.297 | 18.847 |
| 59 | CB | 11 | -12.421 | 74.537 | 20.152 |
| 60 | N | 12 | -14.310 | 71.549 | 20.860 |
| 61 | CA | 12 | -15.320 | 70.695 | 20.297 |
| 62 | C | 12 | 0.000 | -12.537 | 73.194 |
| 63 | O | 12 | 18.422 | 0.000 | -12.537 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

Table 12

| Backbone 107 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.468 | 86.641 | 22.418 |
| 2 | C | 0 | 16.971 | 86.870 | 22.533 |
| 3 | O | 0 | 16.491 | 87.999 | 22.287 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.260 | 85.796 | 22.868 |
| 6 | CA | 1 | 14.825 | 85.866 | 23.065 |
| 7 | C | 1 | 14.159 | 84.664 | 22.417 |
| 8 | O | 1 | 13.215 | 84.830 | 21.612 |
| 9 | CB | 1 | 14.282 | 87.132 | 22.424 |
| 10 | N | 2 | 14.680 | 83.484 | 22.746 |
| 11 | CA | 2 | 14.125 | 82.241 | 22.248 |
| 12 | C | 2 | 12.597 | 82.381 | 22.089 |
| 13 | O | 2 | 11.931 | 82.822 | 23.038 |
| 14 | CB | 2 | 14.438 | 81.109 | 23.212 |
| 15 | N | 3 | 12.131 | 82.035 | 20.895 |
| 16 | CA | 3 | 10.723 | 82.065 | 20.608 |
| 17 | C | 3 | 10.187 | 80.624 | 20.484 |
| 18 | O | 3 | 10.876 | 79.773 | 19.902 |
| 19 | CB | 3 | 10.472 | 82.818 | 19.314 |
| 20 | N | 4 | 9.010 | 80.419 | 21.065 |
| 21 | CA | 4 | 8.357 | 79.140 | 20.993 |
| 22 | C | 4 | 6.911 | 79.322 | 20.491 |
| 23 | O | 4 | 6.290 | 80.350 | 20.801 |
| 24 | CB | 4 | 8.346 | 78.486 | 22.364 |
| 25 | N | 5 | 6.465 | 78.339 | 19.718 |
| 26 | CA | 5 | 5.120 | 78.340 | 19.212 |
| 27 | C | 5 | 4.131 | 78.069 | 20.363 |
| 28 | O | 5 | 4.469 | 77.306 | 21.280 |
| 29 | CB | 5 | 4.966 | 77.274 | 18.142 |
| 30 | N | 6 | 2.983 | 78.731 | 20.275 |
| 31 | CA | 6 | 1.940 | 78.547 | 21.246 |
| 32 | C | 6 | 0.842 | 77.634 | 20.665 |
| 33 | O | 6 | 0.733 | 77.533 | 19.433 |
| 34 | CB | 6 | 1.341 | 79.890 | 21.628 |
| 35 | N | 7 | 0.115 | 76.994 | 21.573 |
| 36 | CA | 7 | -0.978 | 76.143 | 21.187 |
| 37 | C | 7 | -2.002 | 76.952 | 20.366 |
| 38 | O | 7 | -1.726 | 78.116 | 20.039 |
| 39 | CB | 7 | -1.650 | 75.569 | 22.422 |
| 40 | N | 8 | -3.106 | 76.287 | 20.048 |
| 41 | CA | 8 | -4.175 | 76.921 | 19.326 |
| 42 | C | 8 | -5.514 | 76.242 | 19.676 |
| 43 | O | 8 | -6.165 | 75.692 | 18.775 |

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Table 12 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 44 | CB | 8 | -3.925 | 76.820 | 17.831 |
| 45 | N | 9 | -5.836 | 76.283 | 20.964 |
| 46 | CA | 9 | -7.077 | 75.736 | 21.439 |
| 47 | C | 9 | -7.625 | 74.721 | 20.416 |
| 48 | O | 9 | -7.330 | 74.855 | 19.219 |
| 49 | CB | 9 | -8.090 | 76.849 | 21.649 |
| 50 | N | 10 | -8.358 | 73.746 | 20.940 |
| 51 | CA | 10 | -8.977 | 72.751 | 20.108 |
| 52 | C | 10 | -10.440 | 73.147 | 19.824 |
| 53 | O | 10 | -10.703 | 73.773 | 18.787 |
| 54 | CB | 10 | -8.938 | 71.398 | 20.799 |
| 55 | N | 11 | -11.313 | 72.734 | 20.735 |
| 56 | CA | 11 | -12.708 | 73.067 | 20.635 |
| 57 | C | 11 | -13.493 | 71.860 | 20.085 |
| 58 | O | 11 | -13.050 | 71.253 | 19.099 |
| 59 | CB | 11 | -12.892 | 74.262 | 19.715 |
| 60 | N | 12 | -14.591 | 71.556 | 20.766 |
| 61 | CA | 12 | -15.455 | 70.486 | 20.348 |
| 62 | C | 12 | 0.000 | -12.708 | 73.067 |
| 63 | O | 12 | 18.675 | 0.000 | -12.708 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

Table 13

| Backbone 112 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.408 | 86.726 | 22.399 |
| 2 | C | 0 | 16.919 | 86.606 | 22.121 |
| 3 | O | 0 | 16.449 | 87.028 | 21.041 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.215 | 86.005 | 23.077 |
| 6 | CA | 1 | 14.774 | 85.858 | 22.981 |
| 7 | C | 1 | 14.438 | 84.649 | 22.125 |
| 8 | O | 1 | 14.190 | 84.795 | 20.907 |
| 9 | CB | 1 | 14.176 | 87.097 | 22.337 |
| 10 | N | 2 | 14.470 | 83.480 | 22.761 |
| 11 | CA | 2 | 14.125 | 82.241 | 22.093 |
| 12 | C | 2 | 12.600 | 82.176 | 21.872 |
| 13 | O | 2 | 11.849 | 82.152 | 22.858 |
| 14 | CB | 2 | 14.572 | 81.057 | 22.932 |
| 15 | N | 3 | 12.224 | 82.187 | 20.598 |
| 16 | CA | 3 | 10.839 | 82.083 | 20.230 |
| 17 | C | 3 | 10.319 | 80.669 | 20.557 |
| 18 | O | 3 | 11.133 | 79.744 | 20.692 |
| 19 | CB | 3 | 10.674 | 82.359 | 18.745 |
| 20 | N | 4 | 9.001 | 80.583 | 20.701 |
| 21 | CA | 4 | 8.361 | 79.323 | 20.960 |
| 22 | C | 4 | 6.868 | 79.411 | 20.585 |
| 23 | O | 4 | 6.126 | 80.158 | 21.239 |
| 24 | CB | 4 | 8.500 | 78.961 | 22.429 |
| 25 | N | 5 | 6.516 | 78.676 | 19.537 |
| 26 | CA | 5 | 5.150 | 78.615 | 19.095 |
| 27 | C | 5 | 4.229 | 78.301 | 20.291 |
| 28 | O | 5 | 4.706 | 77.734 | 21.285 |
| 29 | CB | 5 | 4.995 | 77.540 | 18.033 |
| 30 | N | 6 | 2.976 | 78.716 | 20.149 |
| 31 | CA | 6 | 1.986 | 78.455 | 21.158 |
| 32 | C | 6 | 0.948 | 77.449 | 20.621 |
| 33 | O | 6 | 1.060 | 77.031 | 19.459 |
| 34 | CB | 6 | 1.291 | 79.747 | 21.552 |
| 35 | N | 7 | 0.020 | 77.088 | 21.499 |
| 36 | CA | 7 | -1.045 | 76.194 | 21.133 |
| 37 | C | 7 | -2.219 | 76.999 | 20.540 |
| 38 | O | 7 | -2.062 | 78.205 | 20.301 |
| 39 | CB | 7 | -1.517 | 75.422 | 22.353 |
| 40 | N | 8 | -3.314 | 76.286 | 20.301 |
| 41 | CA | 8 | -4.508 | 76.904 | 19.793 |
| 42 | C | 8 | -5.720 | 75.987 | 20.056 |
| 43 | O | 8 | -5.881 | 74.984 | 19.345 |
| 44 | CB | 8 | -4.369 | 77.156 | 18.302 |
| 45 | N | 9 | -6.483 | 76.357 | 21.078 |

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Table 13 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 46 | CA | 9 | -7.676 | 75.631 | 21.417 |
| 47 | C | 9 | -7.858 | 74.446 | 20.447 |
| 48 | O | 9 | -7.297 | 74.482 | 19.341 |
| 49 | CB | 9 | -8.883 | 76.549 | 21.338 |
| 50 | N | 10 | -8.598 | 73.451 | 20.920 |
| 51 | CA | 10 | -8.898 | 72.298 | 20.116 |
| 52 | C | 10 | -10.415 | 72.236 | 19.842 |
| 53 | O | 10 | -11.204 | 72.400 | 20.784 |
| 54 | CB | 10 | -8.455 | 71.034 | 20.832 |
| 55 | N | 11 | -10.740 | 72.040 | 18.569 |
| 56 | CA | 11 | -12.112 | 71.910 | 18.163 |
| 57 | C | 11 | -12.689 | 70.583 | 18.695 |
| 58 | O | 11 | -12.384 | 69.523 | 18.128 |
| 59 | CB | 11 | -12.211 | 71.942 | 16.648 |
| 60 | N | 12 | -13.459 | 70.705 | 19.770 |
| 61 | CA | 12 | -14.109 | 69.563 | 20.354 |
| 62 | C | 12 | 0.000 | -12.112 | 71.910 |
| 63 | O | 12 | 18.708 | 0.000 | -12.112 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

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Table 14

| Backbone 118 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.471 | 86.536 | 22.407 |
| 2 | C | 0 | 16.968 | 86.701 | 22.266 |
| 3 | O | 0 | 16.498 | 87.742 | 21.755 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.246 | 85.665 | 22.686 |
| 6 | CA | 1 | 14.795 | 85.690 | 22.663 |
| 7 | C | 1 | 14.271 | 84.435 | 21.986 |
| 8 | O | 1 | 13.620 | 84.525 | 20.922 |
| 9 | CB | 1 | 14.318 | 86.904 | 21.884 |
| 10 | N | 2 | 14.591 | 83.292 | 22.589 |
| 11 | CA | 2 | 14.125 | 82.013 | 22.093 |
| 12 | C | 2 | 12.591 | 82.045 | 21.934 |
| 13 | O | 2 | 11.881 | 82.067 | 22.951 |
| 14 | CB | 2 | 14.518 | 80.907 | 23.057 |
| 15 | N | 3 | 12.165 | 82.081 | 20.677 |
| 16 | CA | 3 | 10.762 | 82.064 | 20.366 |
| 17 | C | 3 | 10.221 | 80.625 | 20.479 |
| 18 | O | 3 | 11.005 | 79.674 | 20.343 |
| 19 | CB | 3 | 10.536 | 82.588 | 18.958 |
| 20 | N | 4 | 8.925 | 80.541 | 20.756 |
| 21 | CA | 4 | 8.263 | 79.268 | 20.845 |
| 22 | C | 4 | 6.879 | 79.352 | 20.171 |
| 23 | O | 4 | 6.325 | 80.457 | 20.070 |
| 24 | CB | 4 | 8.101 | 78.868 | 22.301 |
| 25 | N | 5 | 6.413 | 78.195 | 19.716 |
| 26 | CA | 5 | 5.115 | 78.103 | 19.106 |
| 27 | C | 5 | 4.061 | 77.755 | 20.177 |
| 28 | O | 5 | 4.217 | 76.737 | 20.866 |
| 29 | CB | 5 | 5.122 | 77.034 | 18.027 |
| 30 | N | 6 | 3.069 | 78.632 | 20.282 |
| 31 | CA | 6 | 1.984 | 78.421 | 21.202 |
| 32 | C | 6 | 1.060 | 77.308 | 20.670 |
| 33 | O | 6 | 1.327 | 76.771 | 19.584 |
| 34 | CB | 6 | 1.192 | 79.706 | 21.374 |
| 35 | N | 7 | 0.048 | 76.997 | 21.472 |
| 36 | CA | 7 | -0.928 | 76.012 | 21.093 |
| 37 | C | 7 | -2.316 | 76.673 | 20.976 |
| 38 | O | 7 | -2.546 | 77.708 | 21.619 |
| 39 | CB | 7 | -0.975 | 74.902 | 22.128 |
| 40 | N | 8 | -3.150 | 76.066 | 20.139 |
| 41 | CA | 8 | -4.496 | 76.535 | 19.959 |
| 42 | C | 8 | -5.484 | 75.538 | 20.596 |
| 43 | O | 8 | -5.163 | 74.343 | 20.680 |
| 44 | CB | 8 | -4.801 | 76.684 | 18.479 |

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Table 14 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 45 | N | 9 | -6.612 | 76.081 | 21.040 |
| 46 | CA | 9 | -7.652 | 75.273 | 21.615 |
| 47 | C | 9 | -8.169 | 74.268 | 20.567 |
| 48 | O | 9 | -8.200 | 74.604 | 19.374 |
| 49 | CB | 9 | -8.795 | 76.156 | 22.087 |
| 50 | N | 10 | -8.513 | 73.083 | 21.059 |
| 51 | CA | 10 | -9.059 | 72.056 | 20.214 |
| 52 | C | 10 | -10.544 | 72.355 | 19.925 |
| 53 | O | 10 | -11.281 | 72.703 | 20.859 |
| 54 | CB | 10 | -8.931 | 70.703 | 20.892 |
| 55 | N | 11 | -10.894 | 72.239 | 18.649 |
| 56 | CA | 11 | -12.254 | 72.439 | 18.229 |
| 57 | C | 11 | -13.135 | 71.287 | 18.754 |
| 58 | O | 11 | -13.091 | 70.187 | 18.183 |
| 59 | CB | 11 | -12.328 | 72.490 | 16.713 |
| 60 | N | 12 | -13.856 | 71.586 | 19.828 |
| 61 | CA | 12 | -14.763 | 70.632 | 20.406 |
| 62 | C | 12 | 0.000 | -12.254 | 72.439 |
| 63 | O | 12 | 18.754 | 0.000 | -12.254 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

Table 15

| Backbone 129 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.495 | 86.291 | 22.091 |
| 2 | C | 0 | 17.099 | 86.364 | 22.686 |
| 3 | O | 0 | 16.668 | 87.449 | 23.137 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.409 | 85.228 | 22.645 |
| 6 | CA | 1 | 15.079 | 85.125 | 23.217 |
| 7 | C | 1 | 14.331 | 83.972 | 22.570 |
| 8 | O | 1 | 13.400 | 84.204 | 21.766 |
| 9 | CB | 1 | 14.313 | 86.412 | 22.964 |
| 10 | N | 2 | 14.767 | 82.758 | 22.900 |
| 11 | CA | 2 | 14.125 | 81.558 | 22.404 |
| 12 | C | 2 | 12.611 | 81.805 | 22.245 |
| 13 | O | 2 | 11.911 | 81.927 | 23.261 |
| 14 | CB | 2 | 14.358 | 80.407 | 23.367 |
| 15 | N | 3 | 12.194 | 81.901 | 20.988 |
| 16 | CA | 3 | 10.803 | 82.082 | 20.676 |
| 17 | C | 3 | 10.173 | 80.727 | 20.297 |
| 18 | O | 3 | 10.650 | 80.085 | 19.349 |
| 19 | CB | 3 | 10.652 | 83.058 | 19.522 |
| 20 | N | 4 | 9.165 | 80.348 | 21.074 |
| 21 | CA | 4 | 8.445 | 79.131 | 20.819 |
| 22 | C | 4 | 7.047 | 79.462 | 20.257 |
| 23 | O | 4 | 6.608 | 80.615 | 20.376 |
| 24 | CB | 4 | 8.305 | 78.330 | 22.102 |
| 25 | N | 5 | 6.442 | 78.450 | 19.647 |
| 26 | CA | 5 | 5.114 | 78.588 | 19.113 |
| 27 | C | 5 | 4.079 | 78.178 | 20.180 |
| 28 | O | 5 | 4.373 | 77.289 | 20.993 |
| 29 | CB | 5 | 4.955 | 77.714 | 17.881 |
| 30 | N | 6 | 2.945 | 78.866 | 20.145 |
| 31 | CA | 6 | 1.864 | 78.568 | 21.044 |
| 32 | C | 6 | 1.193 | 77.243 | 20.630 |
| 33 | O | 6 | 1.658 | 76.606 | 19.673 |
| 34 | CB | 6 | 0.841 | 79.690 | 21.018 |
| 35 | N | 7 | 0.165 | 76.881 | 21.388 |
| 36 | CA | 7 | -0.594 | 75.695 | 21.099 |
| 37 | C | 7 | -2.093 | 76.044 | 21.014 |
| 38 | O | 7 | -2.691 | 76.384 | 22.046 |
| 39 | CB | 7 | -0.369 | 74.657 | 22.184 |
| 40 | N | 8 | -2.610 | 75.977 | 19.793 |
| 41 | CA | 8 | -4.006 | 76.226 | 19.560 |
| 42 | C | 8 | -4.854 | 75.414 | 20.559 |
| 43 | O | 8 | -4.305 | 74.533 | 21.237 |
| 44 | CB | 8 | -4.374 | 75.835 | 18.139 |
| 45 | N | 9 | -6.130 | 75.774 | 20.624 |
| 46 | CA | 9 | -7.058 | 75.079 | 21.473 |
| 47 | C | 9 | -8.093 | 74.330 | 20.610 |

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Table 15 continued

| | Atom Number | Atom type | Position in peptide | x y z | | |
|----|----------------|--------------|------------------------|---------|---------|---------|
| | | | | | | |
| 5 | 48 | O | 9 | -8.797 | 74.974 | 19.819 |
| | 49 | CB | 9 | -7.768 | 76.066 | 22.384 |
| | 50 | N | 10 | -8.107 | 73.013 | 20.781 |
| | 51 | CA | 10 | -9.049 | 72.181 | 20.083 |
| | 52 | C | 10 | -10.358 | 72.962 | 19.848 |
| 10 | 53 | O | 10 | -10.355 | 73.921 | 19.062 |
| | 54 | CB | 10 | -9.337 | 70.929 | 20.893 |
| | 55 | N | 11 | -11.409 | 72.493 | 20.510 |
| | 56 | CA | 11 | -12.689 | 73.142 | 20.432 |
| | 57 | C | 11 | -13.742 | 72.155 | 19.889 |
| | 58 | O | 11 | -13.537 | 71.595 | 18.802 |
| | 59 | CB | 11 | -12.603 | 74.353 | 19.519 |
| | 60 | N | 12 | -14.788 | 71.968 | 20.684 |
| | 61 | CA | 12 | -15.877 | 71.114 | 20.295 |
| | 62 | C | 12 | 0.000 | -12.689 | 73.142 |
| 15 | 63 | O | 12 | 18.488 | 0.000 | -12.689 |
| | 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

Table 16

| Backbone 134 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.230 | 86.312 | 21.629 |
| 2 | C | 0 | 16.891 | 86.341 | 22.345 |
| 3 | O | 0 | 16.627 | 87.271 | 23.139 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.061 | 85.351 | 22.027 |
| 6 | CA | 1 | 14.763 | 85.213 | 22.662 |
| 7 | C | 1 | 14.059 | 83.978 | 22.127 |
| 8 | O | 1 | 12.980 | 84.095 | 21.505 |
| 9 | CB | 1 | 13.913 | 86.434 | 22.357 |
| 10 | N | 2 | 14.693 | 82.828 | 22.345 |
| 11 | CA | 2 | 14.125 | 81.558 | 21.938 |
| 12 | C | 2 | 12.594 | 81.689 | 21.812 |
| 13 | O | 2 | 11.893 | 81.568 | 22.828 |
| 14 | CB | 2 | 14.465 | 80.486 | 22.959 |
| 15 | N | 3 | 12.160 | 81.964 | 20.587 |
| 16 | CA | 3 | 10.756 | 82.068 | 20.300 |
| 17 | C | 3 | 10.144 | 80.658 | 20.176 |
| 18 | O | 3 | 10.693 | 79.826 | 19.439 |
| 19 | CB | 3 | 10.545 | 82.834 | 19.005 |
| 20 | N | 4 | 9.066 | 80.454 | 20.925 |
| 21 | CA | 4 | 8.355 | 79.206 | 20.882 |
| 22 | C | 4 | 7.007 | 79.401 | 20.159 |
| 23 | O | 4 | 6.549 | 80.546 | 20.036 |
| 24 | CB | 4 | 8.111 | 78.697 | 22.292 |
| 25 | N | 5 | 6.463 | 78.283 | 19.690 |
| 26 | CA | 5 | 5.184 | 78.295 | 19.035 |
| 27 | C | 5 | 4.068 | 78.033 | 20.066 |
| 28 | O | 5 | 4.279 | 77.235 | 20.991 |
| 29 | CB | 5 | 5.144 | 77.229 | 17.954 |
| 30 | N | 6 | 2.961 | 78.741 | 19.876 |
| 31 | CA | 6 | 1.814 | 78.572 | 20.726 |
| 32 | C | 6 | 1.146 | 77.213 | 20.434 |
| 33 | O | 6 | 1.584 | 76.513 | 19.510 |
| 34 | CB | 6 | 0.820 | 79.695 | 20.486 |
| 35 | N | 7 | 0.150 | 76.899 | 21.254 |
| 36 | CA | 7 | -0.604 | 75.687 | 21.080 |
| 37 | C | 7 | -2.110 | 76.013 | 21.037 |
| 38 | O | 7 | -2.686 | 76.338 | 22.086 |
| 39 | CB | 7 | -0.319 | 74.729 | 22.223 |
| 40 | N | 8 | -2.658 | 75.944 | 19.829 |
| 41 | CA | 8 | -4.064 | 76.173 | 19.635 |
| 42 | C | 8 | -4.872 | 75.344 | 20.653 |
| 43 | O | 8 | -4.333 | 74.368 | 21.198 |
| 44 | CB | 8 | -4.463 | 75.782 | 18.223 |
| 45 | N | 9 | -6.101 | 75.791 | 20.882 |
| 46 | CA | 9 | -6.993 | 75.097 | 21.769 |

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Table 16 continued

| | Atom | | Position in peptide | x y z | | |
|----|--------|------|------------------------|---------|---------|---------|
| | Number | type | | | | |
| 5 | 47 | C | 9 | -8.036 | 74.312 | 20.948 |
| | 48 | O | 9 | -8.773 | 74.928 | 20.163 |
| | 49 | CB | 9 | -7.698 | 76.089 | 22.679 |
| | 50 | N | 10 | -8.021 | 72.999 | 21.144 |
| | 51 | CA | 10 | -8.966 | 72.137 | 20.488 |
| 10 | 52 | C | 10 | -10.293 | 72.891 | 20.269 |
| | 53 | O | 10 | -10.367 | 73.727 | 19.356 |
| | 54 | CB | 10 | -9.213 | 70.899 | 21.332 |
| | 55 | N | 11 | -11.275 | 72.533 | 21.087 |
| | 56 | CA | 11 | -12.558 | 73.179 | 21.038 |
| | 57 | C | 11 | -13.561 | 72.288 | 20.278 |
| | 58 | O | 11 | -13.243 | 71.836 | 19.167 |
| | 59 | CB | 11 | -12.437 | 74.524 | 20.343 |
| | 60 | N | 12 | -14.696 | 72.054 | 20.925 |
| | 61 | CA | 12 | -15.750 | 71.281 | 20.326 |
| 15 | 62 | C | 12 | 0.000 | -12.558 | 73.179 |
| | 63 | O | 12 | 18.616 | 0.000 | -12.558 |
| | 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

Table 17

| Backbone 141 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.454 | 86.485 | 22.460 |
| 2 | C | 0 | 16.950 | 86.573 | 22.266 |
| 3 | O | 0 | 16.481 | 87.224 | 21.305 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.227 | 85.893 | 23.151 |
| 6 | CA | 1 | 14.776 | 85.918 | 23.128 |
| 7 | C | 1 | 14.252 | 84.663 | 22.452 |
| 8 | O | 1 | 13.601 | 84.752 | 21.387 |
| 9 | CB | 1 | 14.299 | 87.132 | 22.349 |
| 10 | N | 2 | 14.573 | 83.520 | 23.055 |
| 11 | CA | 2 | 14.106 | 82.241 | 22.559 |
| 12 | C | 2 | 12.572 | 82.273 | 22.400 |
| 13 | O | 2 | 11.868 | 82.483 | 23.398 |
| 14 | CB | 2 | 14.499 | 81.135 | 23.523 |
| 15 | N | 3 | 12.141 | 82.099 | 21.156 |
| 16 | CA | 3 | 10.736 | 82.054 | 20.855 |
| 17 | C | 3 | 10.224 | 80.605 | 20.973 |
| 18 | O | 3 | 11.035 | 79.698 | 21.214 |
| 19 | CB | 3 | 10.489 | 82.573 | 19.449 |
| 20 | N | 4 | 8.911 | 80.468 | 20.833 |
| 21 | CA | 4 | 8.289 | 79.172 | 20.868 |
| 22 | C | 4 | 6.823 | 79.286 | 20.405 |
| 23 | O | 4 | 6.108 | 80.179 | 20.882 |
| 24 | CB | 4 | 8.338 | 78.611 | 22.279 |
| 25 | N | 5 | 6.465 | 78.404 | 19.478 |
| 26 | CA | 5 | 5.118 | 78.352 | 18.981 |
| 27 | C | 5 | 4.147 | 78.042 | 20.138 |
| 28 | O | 5 | 4.521 | 77.295 | 21.054 |
| 29 | CB | 5 | 4.999 | 77.280 | 17.911 |
| 30 | N | 6 | 2.972 | 78.656 | 20.055 |
| 31 | CA | 6 | 1.943 | 78.430 | 21.033 |
| 32 | C | 6 | 1.020 | 77.288 | 20.562 |
| 33 | O | 6 | 1.265 | 76.719 | 19.488 |
| 34 | CB | 6 | 1.130 | 79.697 | 21.234 |
| 35 | N | 7 | 0.034 | 76.991 | 21.401 |
| 36 | CA | 7 | -0.938 | 75.983 | 21.081 |
| 37 | C | 7 | -2.338 | 76.622 | 20.985 |
| 38 | O | 7 | -2.577 | 77.649 | 21.637 |
| 39 | CB | 7 | -0.939 | 74.903 | 22.150 |
| 40 | N | 8 | -3.173 | 76.006 | 20.156 |
| 41 | CA | 8 | -4.529 | 76.453 | 19.995 |
| 42 | C | 8 | -5.492 | 75.437 | 20.641 |
| 43 | O | 8 | -5.144 | 74.250 | 20.729 |
| 44 | CB | 8 | -4.856 | 76.604 | 18.520 |
| 45 | N | 9 | -6.629 | 75.957 | 21.087 |
| 46 | CA | 9 | -7.649 | 75.129 | 21.670 |
| 47 | C | 9 | -7.625 | 73.734 | 21.014 |

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Table 17 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 48 | O | 9 | -6.531 | 73.205 | 20.765 |
| 49 | CB | 9 | -9.013 | 75.766 | 21.470 |
| 50 | N | 10 | -8.822 | 73.200 | 20.803 |
| 51 | CA | 10 | -8.965 | 71.925 | 20.155 |
| 52 | C | 10 | -10.460 | 71.616 | 19.939 |
| 53 | O | 10 | -11.065 | 70.945 | 20.788 |
| 54 | CB | 10 | -8.334 | 70.836 | 21.005 |
| 55 | N | 11 | -10.983 | 72.148 | 18.840 |
| 56 | CA | 11 | -12.353 | 71.910 | 18.476 |
| 57 | C | 11 | -12.732 | 70.452 | 18.805 |
| 58 | O | 11 | -12.400 | 69.551 | 18.020 |
| 59 | CB | 11 | -12.548 | 72.168 | 16.992 |
| 60 | N | 12 | -13.373 | 70.294 | 19.958 |
| 61 | CA | 12 | -13.836 | 69.000 | 20.380 |
| 62 | C | 12 | 0.000 | -12.353 | 71.910 |
| 63 | O | 12 | 18.541 | 0.000 | -12.353 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

Table 18

| Backbone 144 | | | | | |
|----------------|--------------|------------------------|--------|--------|--------|
| Atom Number | Atom type | Position in peptide | x | y | z |
| 0 | N | 0 | 0.000 | 0.000 | 0.000 |
| 1 | CA | 0 | 18.480 | 86.428 | 22.392 |
| 2 | C | 0 | 16.967 | 86.551 | 22.343 |
| 3 | O | 0 | 16.431 | 87.361 | 21.553 |
| 4 | CB | 0 | 0.000 | 0.000 | 0.000 |
| 5 | N | 1 | 16.308 | 85.727 | 23.153 |
| 6 | CA | 1 | 14.861 | 85.759 | 23.256 |
| 7 | C | 1 | 14.262 | 84.643 | 22.416 |
| 8 | O | 1 | 13.512 | 84.919 | 21.454 |
| 9 | CB | 1 | 14.341 | 87.091 | 22.745 |
| 10 | N | 2 | 14.630 | 83.412 | 22.767 |
| 11 | CA | 2 | 14.106 | 82.241 | 22.093 |
| 12 | C | 2 | 12.565 | 82.287 | 22.092 |
| 13 | O | 2 | 11.968 | 82.501 | 23.158 |
| 14 | CB | 2 | 14.581 | 80.981 | 22.796 |
| 15 | N | 3 | 12.006 | 82.121 | 20.899 |
| 16 | CA | 3 | 10.578 | 82.090 | 20.743 |
| 17 | C | 3 | 10.094 | 80.628 | 20.667 |
| 18 | O | 3 | 10.880 | 79.754 | 20.273 |
| 19 | CB | 3 | 10.177 | 82.830 | 19.479 |
| 20 | N | 4 | 8.846 | 80.435 | 21.077 |
| 21 | CA | 4 | 8.236 | 79.135 | 21.020 |
| 22 | C | 4 | 6.879 | 79.228 | 20.292 |
| 23 | O | 4 | 6.338 | 80.337 | 20.167 |
| 24 | CB | 4 | 8.027 | 78.596 | 22.424 |
| 25 | N | 5 | 6.422 | 78.073 | 19.822 |
| 26 | CA | 5 | 5.148 | 77.990 | 19.162 |
| 27 | C | 5 | 4.052 | 77.645 | 20.190 |
| 28 | O | 5 | 4.068 | 76.532 | 20.737 |
| 29 | CB | 5 | 5.192 | 76.923 | 18.081 |
| 30 | N | 6 | 3.184 | 78.622 | 20.423 |
| 31 | CA | 6 | 2.076 | 78.436 | 21.319 |
| 32 | C | 6 | 1.134 | 77.348 | 20.765 |
| 33 | O | 6 | 1.402 | 76.819 | 19.676 |
| 34 | CB | 6 | 1.313 | 79.740 | 21.481 |
| 35 | N | 7 | 0.109 | 77.048 | 21.553 |
| 36 | CA | 7 | -0.883 | 76.089 | 21.152 |
| 37 | C | 7 | -2.256 | 76.780 | 21.027 |
| 38 | O | 7 | -2.407 | 77.911 | 21.512 |
| 39 | CB | 7 | -0.965 | 74.968 | 22.174 |
| 40 | N | 8 | -3.167 | 76.084 | 20.357 |
| 41 | CA | 8 | -4.509 | 76.574 | 20.198 |
| 42 | C | 8 | -5.503 | 75.588 | 20.843 |
| 43 | O | 8 | -5.193 | 74.391 | 20.931 |
| 44 | CB | 8 | -4.832 | 76.735 | 18.722 |

Table 18 continued

| Atom Number | Atom type | Position in peptide | x | y | z |
|----------------|--------------|------------------------|---------|---------|---------|
| 45 | N | 9 | -6.623 | 76.144 | 21.290 |
| 46 | CA | 9 | -7.669 | 75.348 | 21.873 |
| 47 | C | 9 | -8.201 | 74.343 | 20.832 |
| 48 | O | 9 | -8.407 | 74.731 | 19.672 |
| 49 | CB | 9 | -8.801 | 76.243 | 22.347 |
| 50 | N | 10 | -8.360 | 73.106 | 21.286 |
| 51 | CA | 10 | -8.894 | 72.067 | 20.448 |
| 52 | C | 10 | -10.383 | 72.344 | 20.162 |
| 53 | O | 10 | -11.124 | 72.681 | 21.097 |
| 54 | CB | 10 | -8.745 | 70.719 | 21.133 |
| 55 | N | 11 | -10.734 | 72.224 | 18.886 |
| 56 | CA | 11 | -12.097 | 72.403 | 18.469 |
| 57 | C | 11 | -12.907 | 71.126 | 18.774 |
| 58 | O | 11 | -12.859 | 70.178 | 17.977 |
| 59 | CB | 11 | -12.150 | 72.700 | 16.980 |
| 60 | N | 12 | -13.575 | 71.155 | 19.921 |
| 61 | CA | 12 | -14.414 | 70.059 | 20.322 |
| 62 | C | 12 | 0.000 | -12.097 | 72.403 |
| 63 | O | 12 | 18.465 | 0.000 | -12.097 |
| 64 | CB | 12 | 0.000 | 0.000 | 0.000 |

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Example 4

The following method was used to identify high affinity binding peptides from Myelin Basic Protein (MBP). The binding
5 affinities for a set of MBP peptides to HLA-DRB1*0401 have been experimentally determined and published. This set includes all possible 13 amino acid peptides from the MBP sequence which have a hydrophobic anchor residue at the P3 position. It is known that only such peptides bind to HLA-DR
10 molecules with detectable affinity.

The same homology model of HLA-DRB1*0401 was used for this example as was used in Examples 1 and 2.

15 For each of the 13-mer peptides from the experimental determined set, a binding score was calculated as follows:

a) Calculate the steric overlap between the pocket bound peptide residue in the binding groove and an atom forming the
20 pocket; this is value B.

b) Count the number of hydrogen bonds which could be formed between the pocket bound peptide residue and atoms forming the pocket; this is value C.
25

c) Calculate the strength of electrostatic interactions between any polar atoms of the pocket bound peptide residue and any polar atoms forming the pocket; this is value D.

30 d) Count the number of favourable contacts between the pocket bound peptide residue and atoms forming the pocket; this is value E.

e) These values were then transformed into a conformation
35 score (Z) by using the following equation:

$$Z_n = cK_2C - cK_3D + cK_4E - cK_1B$$

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Where K_1 to K_4 are constants and n is the sequence position of the peptide residue (numbered from 1 to the N-terminus to 13 at the C-terminus). K_1 , K_2 , K_3 and K_4 are equal to 100, 1500, 500 and 1000, respectively.

5

The conformation of each rotatable side-chain of the peptide residue was then altered by 15 degrees and the conformation score was recalculated.

- 10 The above steps were repeated for each residue of the peptide and the highest conformation score for each peptide residue was used to determine the conformation score for the peptide.

At the point, the entire proceedings for establishing the
15 conformation score for the peptide were repeated another 166 times, each time using a different peptide backbone from the library of peptide backbones.

The combination of peptide backbone and peptide side-chain
20 conformations which gave the best conformation was then used to determine a binding score for the peptide.

The binding score was determined by establishing values of the following parameters:

25

- a) Calculate the steric overlap between the pocket bound peptide residue in the binding groove and an atom forming the pocket; this is value B.
- 30 b) Count the number of hydrogen bonds which could be formed between the pocket bound peptide residue and atoms forming the pocket; this is value C.
- c) Calculate the strength of electrostatic interactions
35 between any polar atoms of the pocket bound peptide residue and any polar atoms forming the pocket; this is value D.

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- d) Count the number of favourable contacts between the pocket bound peptide residue and atoms forming the pocket; this is value E.
- 5 e) Calculate the hydrophobicity of the pocket bound peptide side chains using a hydrophobicity scale disclosed in Janin et al.
- f) Calculate the number of MHC pocket residues which are
10 paired with the pocket bound peptide residues. Pairing takes place if the centre of an atom from the MHC pocket residue and the centre of an atom from the pocket bound peptide residues are no more than the sum of their van der wall radii plus one Angstrom. The value A_n is calculated by summing the number of
15 paired residues, where n is the number of the pocket. The values of A_n taking into account the pockets importance in binding are summed to give a value P.

The above values were then imported in to the following
20 equation in order to determine the binding score (Y):

$$Y=P+bK_2C-bK_3D+bK_4E-bK_1B+bK_5He$$

Wherein the values bK_1 , bK_2 , bK_3 , bK_4 and bK_5 are 2, 40, 600,
25 10 and 200 respectively.

As can be seen from the results in Table 19 the top four predicted scores pertain to four peptides which appear within the top five best binders.

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Table 19

| BB | PEPTIDE | AFFINITY | BINDING SCORE | D | E | F | B | P | Hc |
|-----|----------------|----------|------------------|-------|----|----|-------|------|------|
| 104 | HFFKNIVTPRTPP | 40 | 4729 | -0.12 | 11 | 17 | 97.7 | 3580 | 1.5 |
| 107 | VHFFKNIVTPRTP | 135 | 2125 | -0.19 | 12 | 15 | 284.5 | 2255 | 0.2 |
| 104 | PVHFFKNIVTPR | 161 | 4528 | -0.06 | 15 | 12 | 337.6 | 4565 | 1.4 |
| 104 | FSWGAEGQRPGFG | 298 | 5205 | -0.15 | 12 | 10 | 169.7 | 4670 | -0.2 |
| 104 | KGFKGVDAQGTL | 480 | 4353 | -0.09 | 9 | 13 | 88.2 | 3145 | 1.9 |
| 112 | KYLATASTMDHAR | 479 | 2672 | -0.09 | 13 | 15 | 106.8 | 1480 | 2.4 |
| 129 | SKYLATASTMDHA | 601 | 498 | -0.08 | 11 | 13 | 275.7 | 620 | 0.4 |
| 141 | RGLSLSRFSWGAE | 1213 | 4140 | -0.05 | 17 | 16 | 81.4 | 3455 | 1.7 |
| 62 | TGILDSIGRFFGG | 2942 | 337 | 0.04 | 21 | 17 | 25.3 | -5 | -0.6 |
| 0 | RFFGGDRGAPKRG | 3403 | 3218 | -0.24 | 20 | 14 | 389.1 | 3100 | 1.6 |
| 104 | NIVTPRTPPPSQG | 6615 | 1971 | 0 | 10 | 11 | 305 | 2090 | 0.8 |
| 14 | DSIGRFFGGDRGA | 7268 | 1904 | -0.08 | 8 | 15 | 37.3 | 1640 | 0.2 |
| 0 | SRFSWGAEGQRPG | 8352 | 1735 | -0.08 | 20 | 13 | 466.8 | 1965 | 0.8 |
| 104 | SKIFKLGGDRSRS | 8494 | 1387 | -0.1 | 10 | 10 | 149.2 | 825 | 2.8 |
| 118 | SDYKSAHKGFKGV | 8510 | 1864 | -0.27 | 14 | 14 | 14.2 | 775 | 0.7 |
| 65 | STMDHARHGFLPR | 8860 | 1888 | -0.21 | 14 | 15 | 191.3 | 1410 | 2.2 |
| 104 | NPVHFFKNIVTP | 12870 | 1347 | -0.11 | 12 | 10 | 332.5 | 1690 | 0.2 |
| 104 | GTLSKIFKLGGRD | 16000 | 4152 | -0.11 | 17 | 10 | 118 | 3775 | 1.1 |
| 93 | GRFFGGDRGAPKR | 18467 | 244 | -0.11 | 8 | 9 | 161 | -175 | 2.3 |
| 75 | KIFKLGGDRDSRSG | 25358 | 2185 | -0.13 | 19 | 12 | 279.4 | 2060 | 1.4 |
| 0 | FGYGGRASDYKSA | 26397 | 1301 | -0.12 | 15 | 15 | 306.1 | 1630 | -0.4 |
| 0 | PGFGYGGRASDYK | 35200 | 3485 | 0.01 | 14 | 13 | 183.5 | 3165 | 1.4 |
| 144 | GILDSIGRFFGGD | 44400 | 2031 | -0.09 | 21 | 14 | 32.1 | 1745 | -0.5 |
| 134 | KNIVTPRTPPPSQ | 59000 | 1077 | -0.04 | 9 | 10 | 45.9 | 340 | 3.1 |
| 0 | KGVDAQGTLSKIF | 100000 | 2067 | -0.11 | 24 | 15 | 695.2 | 2795 | 0.3 |

KEY - BB = NUMBER OF THE BACKBONE CHOSEN FROM THE LIBRARY

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CLAIMS

1. A method for the prediction of the binding affinity of a peptide to a major histocompatibility (MHC) class II molecules comprising;
 - a) ascertaining the characteristics of a MHC molecule binding groove,
 - b) presenting a selected peptide to the MHC molecule and ascertaining a first conformation score for each pocket bound peptide side-chain,
 - c) amending the conformation of each pocket bound peptide side-chain and ascertaining a second conformation score,
 - d) repeating step 3 with alternative conformations of each peptide pocket bound side-chain,
 - e) choosing the highest conformation score for each pocket bound peptide side-chain in each binding groove pockets, herein known as 'the pocket', and
 - f) combining the highest conformation score for each pocket and ascertaining a binding score for the complete peptide.
2. A method according to claim 1 which further comprises the step of compiling information on all peptide fragments in a protein and comparing the binding scores.
3. A method according to any preceding claim wherein the conformation score is ascertained by at least one of the following parameters:
 - a) the number of favourable contacts between MHC residues forming one of the pockets and the pocket bound peptide residue; this is value E
 - b) the steric overlap between the pocket bound peptide residue bound in the pocket and an atom forming the pocket; this is value B,
 - c) the number of hydrogen bonds which could be formed between the pocket bound peptide residue and an atom forming the pocket; this is value C,
 - d) the strength of electrostatic interactions between any

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polar atoms of the pocket bound peptide residue and any polar atoms forming the pocket; this is value D.

4. A method according to claim 3 wherein the steric overlap
5 between the pocket bound peptide residue and the atoms forming the pocket can not be greater than 0.35 Angstroms.

5. A method according to claim 3 wherein a favourable
contact occurs when an atom from an MHC residue and an atom
10 from the peptide residue have their centres separated by no more than the sum of their radii plus 0.5 Angstroms and are not overlapping.

6. A method according to the preceding claims wherein values
15 B to E are imported into a first equation, to give a conformation score (Z)

7. A method according to claim 6 wherein the first equation
is $Z_n = (cK_2C) - (cK_3D) + (cK_4E) - (cK_1B)$, where cK_1 to cK_4 are
20 constants and n is the number of the pocket.

8. A method according to claim 7 wherein cK_1 is between 50 and 150.

25 9. A method according to claim 7 wherein cK_2 is between 1000 and 2000.

10. A method according to claim 7 wherein cK_3 is between 250 and 750.

30

11. A method according to claim 7 wherein cK_4 is between 500 and 1500.

12. A method according to any preceding wherein the Z_n value
35 for a pocket is multiplied by a coefficient, L, depending on the pockets importance in binding, to give a second Z_n value.

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13. A method according to any of the preceding claims wherein all the Z values are summed to give a value J.

14. A method according to any of the preceding claims wherein the MHC residue is paired with the pocket-bound peptide residue if an atom from the MHC residue and an atom from the pocket-bound peptide residue have their centres separated by no more than the sum of their van der Waal radii plus one Angstrom.

10

15. A method according to claim 14 wherein a value A_n is calculated by summing the pairwise interaction frequencies of paired residues.

15 16. A method according to either claim 14 or 15 wherein the value A_n for a pocket is multiplied by a coefficient, X, depending on the pockets importance in binding.

17. A method according to claim 16 wherein the A_n value for the pockets are summed to give a value P.

18. A method according to any preceding claim wherein the binding score is ascertained by at least one of the following parameters

25 a) the number of groove-bound hydrophobic residues; this is value F,

b) the number of non groove-bound hydrophilic residues; this is value G,

30 c) the number of peptide residues deemed to fit within their respective binding pocket; this is value H.

19. A method according to any one of claims 13 to 18 wherein values F, G, H, J and P are imported into a second equation to give a first binding score, Y.

35

20. A method according to claim 19 wherein the second algorithm is $Y = J * F^2 * (G * H + 1) + P$.

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21. A method according to claim 1-17 wherein the hydrophobicity of the pocket bound peptide side chains is evaluated using a hydrophobicity scale; this is value H_e .
- 5 22. A method according to claim 21 wherein the hydrophobicity scale ranges from -1.8 for lysine to 0.9 for cysteine.
23. A method according to either of claims 21 or 22 wherein $Y = (bK_2C) - (bK_3D) + (bK_4E) - (bK_1B) + (bK_5H_e) + P$.
- 10 24. A method according to claim 23 wherein bK_1 is between 1 and 5.
25. A method according to claim 23 wherein bK_2 is between 20
15 and 60.
26. A method according to claim 23 wherein bK_3 is between 300 and 900.
- 20 27. A method according to claim 23 wherein bK_4 is between 1 and 20.
28. A method according to claim 23 wherein bK_5 is between 1 and 800.
- 25 29. A method according to any preceding claim wherein the steps in claim 3 are repeated for each pocket and each conformation of the peptide residue in said pocket.
- 30 30. A method according to claim 29 wherein the conformation of the peptide is altered by rotating a side chain of the peptide residue by a pre-determined amount.
- 35 31. A method according to either claim 29 or 30 where in the conformation of the peptide is altered by changing the conformation of the peptide backbone.

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32. A method according to any preceding claim wherein the steps are repeated using different peptides from a protein.
33. A method according to any of the preceding claim wherein
5 the binding scores (Y) for different peptides are tabulated and compared.
34. A method according to any of the preceding claim which is used in the manufacture of a vaccine derived from a peptide
10 identified by said method.
35. A method according to any of the preceding claims which is used to remove potentially immunogenic sequences from a protein and thus reduce said proteins immunogenicity when
15 administered to an organism.
36. A computer conditioned to receive information characterising a peptide bound to the MHC molecule and to utilise said information to perform a procedure having the
20 following steps;
- a) ascertaining the characteristics of a MHC molecule binding groove;
 - b) presenting a selected peptide, which is selected by a predetermined program, to the MHC molecule and ascertaining
25 a first conformation score;
 - c) amending the conformation of the peptide, by way of a predetermined program, and ascertaining a second conformation score;
 - d) repeating step 3 with other conformations of the peptide;
 - 30 e) selecting the peptide conformation with the highest conformation score; and
 - f) calculating the binding score from the conformation score.
37. A computer according to claim 36 further comprising a
35 step (7) which comprises repeating steps 1-4 with other peptide fragments in the protein
to generate information on all peptide fragments in a protein

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so that a comparison can be made of the strength of the binding between the peptide and the MHC molecule.

38. A computer according to either claim 36 or 37 further
5 comprising a step (8) which comprises altering the conformation of the backbone of the peptide fragment.

39. A pharmaceutical composition produced resultant upon to a method as claimed in anyone of claims 1 to 35.

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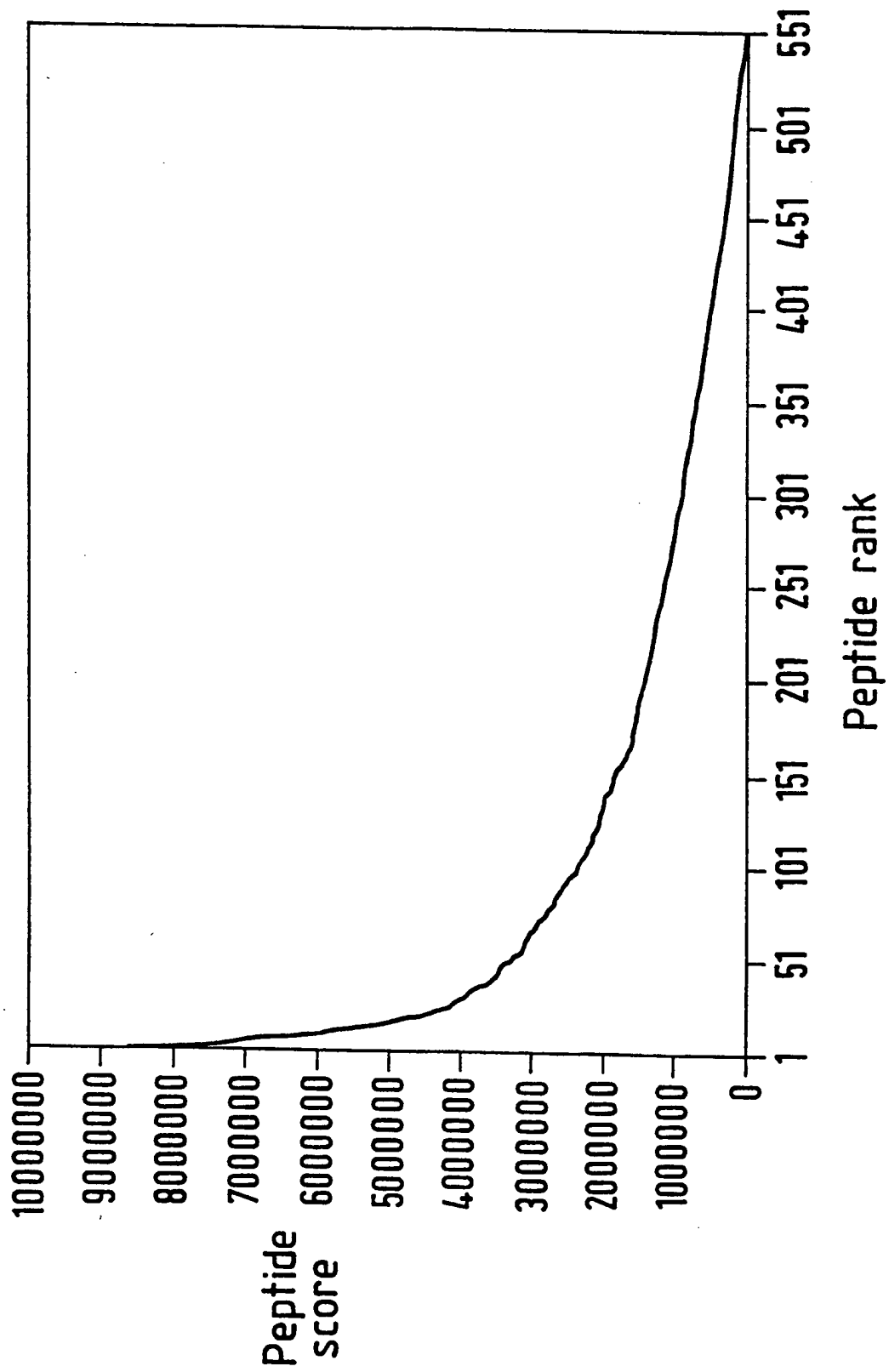
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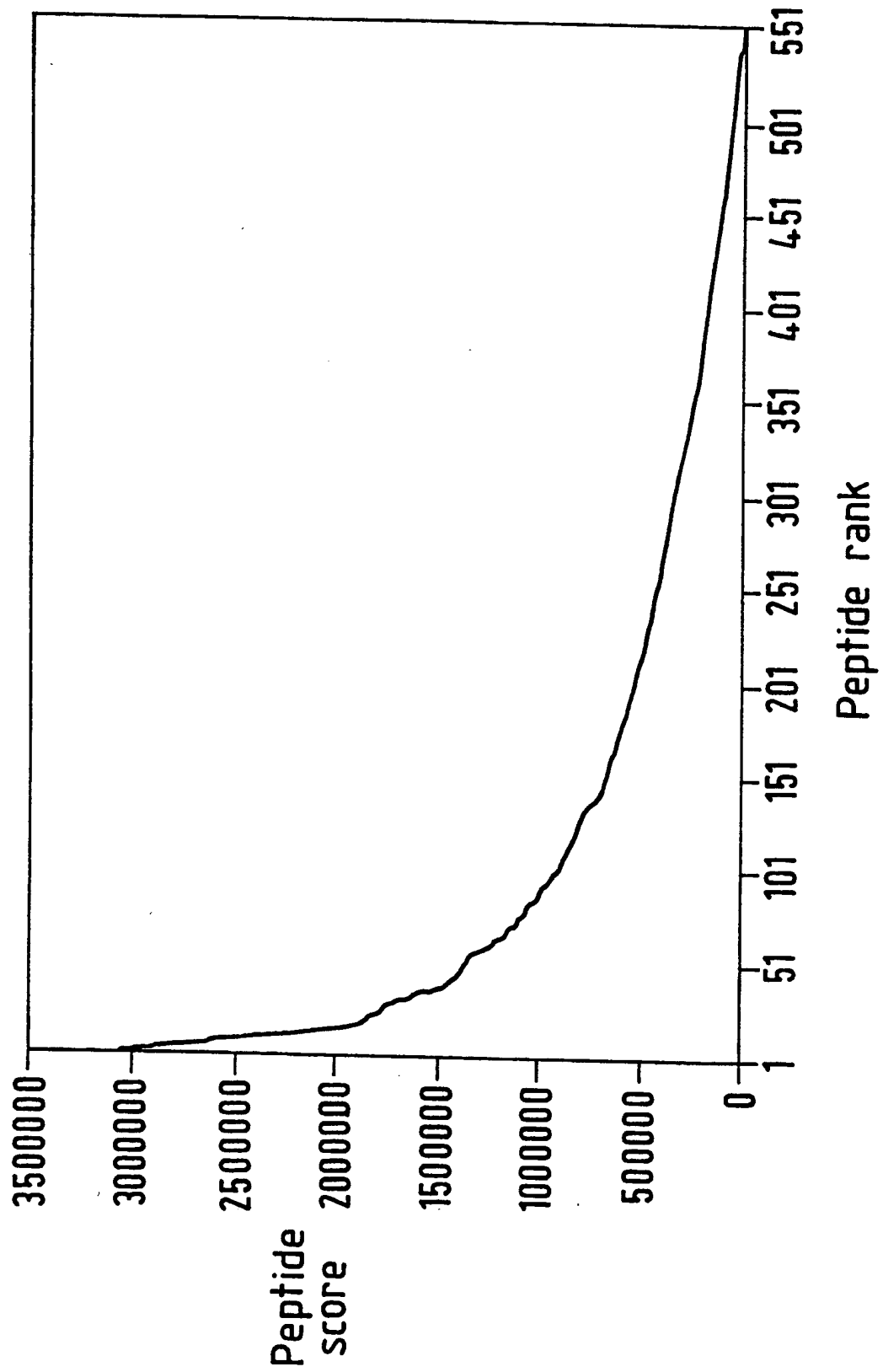
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FIG. 1



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FIG. 2



INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 98/01801

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 G01N33/569 G01N33/564 G01N33/566 C07K14/705

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|--|-----------------------|
| A | WO 95 31483 A (ECLAGEN LTD) 23 November 1995 see page 2, line 23 - line 28 see page 5, line 5 - line 12 | 1-35 |
| X | --- | 39 |
| X,P | WO 97 40852 A (ANERGEN INC) 6 November 1997 see claims 31,32 | 39 |
| A,P | --- | 1-35 |
| | -/-- | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

22 October 1998

Date of mailing of the international search report

05/11/1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|-----------------------|
| T | <p>T.E. JOHANSEN ET AL.: "Peptide binding to MHC class I is determined by individual pockets in the binding groove." SCANDINAVIAN JOURNAL OF IMMUNOLOGY, vol. 46, no. 2, 1 August 1997, pages 137-146, XP002081826 oxford uk see the whole document -----</p> | 1-35, 39 |

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 98/01801

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 36-38
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(i) PCT - Mathematical method
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 98/01801

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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| | | CA 2190101 A | 23-11-1995 |
| | | EP 0759944 A | 05-03-1997 |
| | | JP 10500670 T | 20-01-1998 |
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